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Comparative Morbidity and Mortality of Antimicrobially Treated and Untreated Idiopathic Effusion in the Negro*

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Serofibrinous pleurisy with effusion is usually a manifestation of inflammatory disease adjacent to the pleura. It has been the custom to identify these effusions according to their underlying etiology, which ordinarily becomes apparent after the usual clinical and laboratory examinations. Pulmonary infarction, primary and metastatic pulmonary and pericardial neoplasms, pyogenic pneumonitidies, lung abscess, various viral and mycotic infections, sarcoidosis, diffuse collagen diseases, the migratory phase of certain nematode infections, and tuberculosis have all been known to produce serofibrinous effusions at one time or another during the course of the disease process. We have chosen to retain the term idiopathic pleural effusion for those serofibrinous fluids whose etiology has remained undetermined after the initial clinical and laboratory investigations.

It is agreed by phthisiologists that idiopathic pleural effusion is most likely due to tuberculosis. This assumption has been justified by the results of careful follow-up of the post-pleuritic patient. Some studies by thoracoscopy, thoracotomy, and needle biopsy of the pleura have, in general, tended to reinforce the follow-up studies.

Our study was initiated in 1947 at the beginning of the antimicrobial management of tuberculosis at our institution. At that time, it was the consensus of authority that primary tuberculosis, primary tuberculous pleural effusion, and minimal reinfection pulmonary tuberculosis should not be treated with streptomycin. This opinion was based principally on the belief that the toxicity of streptomycin and the dangers of streptomycin-resistant tuberculosis out-weighed the advantages of antimicrobial treatment for forms of the disease that might be managed satisfactorily without chemotherapy. This attitude seemed unreasonable to the senior author.

When review of the American literature subsequent to 1925 disclosed no statistically valid study of the medical course of Negroes who had suffered an idiopathic pleural effusion, and only two studies which shed any light upon the comparative tuberculous morbidity and mortality

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in the post-effusion Negro and Caucasian, it was decided to make a controlled study of the course and prognosis of antimicrobially treated idiopathic pleural effusion in the American Negro.

Any Negro of post-pediatric age who was admitted with, or developed while hospitalized, a pleural effusion extensive enough to more than obscure the costophrenic sinus on the erect roentgenogram was given consideration for admission to one of the study groups. If the fluid persisted for more than two weeks, and no definite or reasonable diagnosis could be made by clinical or laboratory study, the effusion was considered an idiopathic one. Effusions accompanying congestive failure or renal disease, post-operative effusions, and those with x-ray evidence of active pulmonary disease of any type were all excluded. Because of general opposition to the treatment of idiopathic pleural effusions with antimicrobials, we required that all patients admitted to either the treated or untreated group have a positive tuberculin reaction either at the time of admission or within a few weeks of the initial ward studies. When these criteria were met, the patient could be antimicrobially treated or untreated more or less at the option of the ward physician.

The control group consisted of 47 Negroes with idiopathic pleural effusion who were followed for a minimum of five years, or until active

DISTRIBUTION BY:		UNTREATED (47)	TREATED (45)
SEX	MALE	21	19
	FEMALE	26	26
AGE	11–20	3	9
	21–30	18	14
	31–40	8	8
	41–50	8	11
	51–60	6	3
	61–70	3	0
	71–80	1	0
POSITION OF EFFUSION	Right	23	27
	Left	21	13
	Bilateral	3	5
	Polyserositis	3	7
GRADE * OF EFFUSION	1	22	22
	2	19	20
	3	8	9
CULTURE OF EFFUSION	M. Tuberc. found	4	9
	M. Tuberc. not found	39	33
KNOWN CONTACT	Intimate expos. to tuberculosis	15	10
	Deaths in family from tuberculosis	7	6

FIGURE 1: Composition of the two study groups. *Grade of effusion: grade 1 effusions extended up to the inferior margin of the second rib anteriorly; those of grade 2 extended above the inferior margin of rib four but below rib two, and grade 3 fluids did not reach the inferior margin of rib four anteriorly.

tuberculosis appeared, and four patients who were not adequately followed.

The antimicrobially treated group contained 47 Negroes with idiopathic pleural effusion, only two of whom could not be followed. Forty-four were followed for five or more years, or until death, and one was lost after four years. The two groups were surprisingly uniform according to sex, age, size and position of effusion, contact history, and the results of culture of the effusion. Figure 1 is a tabulation of these data. The conditions surrounding hospitalization were as uniform for the two groups as can be obtained when a single hospital population is being used without imposing special rules for management.

Effusion into the right hemi-thorax occurred more frequently than into the left, which is in agreement with most studies of the distribution of tuberculous primary effusion. The incidence of effusion into more than one serous space was surprisingly high. In the combined series of treated and untreated, bilateral pleural effusion was present in 8.7 per cent and polyserositis in 10.8 per cent, giving an incidence of 19.5 for effusion into more than one serous space. This is considerably higher than in studies of Caucasians, and is, we believe, an expression of basic differences in host-parasite relationships between the American Negro and Caucasian.

After discharge from hospital, the patients were kept under periodic observation in the out-patient clinic. X-ray films were obtained, usually

DISTRIBUTION OF RESULTS ACCORDING TO DURATION OF ANTIMICROBIAL THERAPY

DURATION OF TREATMENT IN DAYS	NUMBER WELL	NUMBER RELAPSING	NUMBER DYING
30-35	3	1	
42	6	4	
60	5		
61-90	3	1	1
91-120	5		
121-190	9	1	
270-365	3		1
Over 365	2		

FIGURE 2: See text for definitions of "well" and "relapse." Does not include patient with disseminated lupus.

at two or three month intervals for the first one to two years, and at intervals of three to six months thereafter. Most of those who relapsed during the period of observation were readmitted to the tuberculosis service for further care. Follow-up of Negro patients is frequently difficult, and delinquency among the men is common. Much of our success in follow-up is due to the active assistance of the Social Service Department of Charity Hospital and the Welfare Agency of the State. The serial x-ray films for each patient were reviewed at a single time for evaluation at the conclusion of the study.

There was considerable variation in the antimicrobial treatment given. Figure 2 shows the distribution of therapy according to duration. Most of those who received no more than 60 days of treatment were given one gram of streptomycin or dihydrostreptomycin daily. The total dose of antimicrobials was quite variable among those receiving treatment beyond 60 days. Some of the latter received one gram of streptomycin or dihydrostreptomycin daily, some received one gram of the antibiotic three times a week, some received it on two days of each week, and some received streptomycin or dihydrostreptomycin daily for several weeks and were then placed on intermittent schedules. Because of this lack of uniformity, patients are classified according to duration of treatment only. In general, the treatment used reflected current protocols of the Veterans Administration-Army-Navy cooperative study. Streptomycin was not available to us during the time of the initial Veterans Administration studies which prescribed one or two grams daily for 120 days. Not all of our patients received paraminosalicylic acid. No statistical separation was made between those receiving streptomycin alone and those receiving both the antibiotic and PAS.

Results

We have tabulated the findings which we believe to be of greatest interest in Figures 2 - 6. The data are presented in a form that permits easy comparison with the observations of others.

MORBIDITY AND MORTALITY FROM TUBERCULOSIS IN POSTPLEURITIC NEGROES

AUTHOR AND YEAR	NUMBER OF NEGROES WITH EFFUSION	PERCENTAGE FOLLOW-UP	DURATION OF FOLLOW-UP	PERCENTAGE DEVELOPING TUBERCULOSIS	PERCENTAGE DYING FROM TUBERCULOSIS
Bonilla (1942)	29	100	31.9 months *	37.9	20.7
Farber (1943)	30*	81*	3-13 years	56.	?
Jones and Dooley (1946)	106 (69 males)	69	12-18 months	?	about 16.6
Present series untreated	51	92	5 or more years	64.	21.3
Present series treated	47	95.7	4-9 years	17.7	4.4

* Mean follow-up for the group.

* Follow-up for 3-13 years on 81% of the total series, white and colored. Author did not specify the percentage follow-up for each racial group, but 30 Negroes were followed from 3-13 years.

FIGURE 3: All studies of the American Negro which are suitable for statistical study are included.

Figure 3 depicts the morbidity and mortality in both the treated and untreated groups. It includes for easy comparison data from all suitable studies of primary pleural effusion in the American Negro which we could find. The incidence of tuberculosis in all untreated groups is high, and among our treated group, it is significantly lower. There is a more striking contrast between the high mortality of the untreated group and the mortality in the treated group. Although the difference in both morbidity and mortality between the untreated and treated is quite significant, this significance must be interpreted in the light of the type of antimicrobial treatment given.

The considerable variation in antimicrobial treatment given has already been discussed. Inspection of Figure 2 will show that most of the antimicrobial treatment was inadequate by present day standards. Twenty-three of the patients received treatment for somewhere between 30 and 90 days, and 26 per cent of them relapsed. Twenty-one were treated for more than 90 days, and 9.5 per cent relapsed; both of these relapses were due to miliary-meningeal tuberculosis, one of which was fatal. This difference is not statistically significant.

It is interesting to compare these results in Negroes with the selected studies of Caucasians tabulated in Figure 7. With the exception of Thompson's study, the postpleuritic morbidity is about the same as in our Negroes, and the percentage of relapse in Roper and Waring's study is almost identical. The mortality rate is much lower in the Caucasian group than in the Negro. The high rate in Pätiälä's series may be due

SUMMARY OF COURSE OF 45 ANTIMICROBIALLY TREATED AND 47 UNTREATED NEGROES DURING POSTPLEURITIC FOLLOW-UP

STATUS		UNTREATED			TREATED		
		No.	%		No.	%	
WELL	without scar by x-ray	8	17.		20	44.4	
	with scar by x-ray	4	8.5		9	20.	
	with active disease by x-ray	5	10.6		7	15.5	
DEAD	from tuberculosis	7	15.	21.3	2	4.4	4.4
	with tuberculosis	3*	6.3		0	0.	
	from other causes	0	0		1	2.2	
ALIVE	with active tuberculosis	20	42.5		6	13.3	

* Tuberculosis a significant cause of death in one of these

FIGURE 4: See text for definition of terms.

to the severity of war-time conditions in Finland. The striking difference in postpleuritic mortality among Caucasians and Negroes can be explained by the studies of Pinner and Kasper[1] and Rich.[2] Their studies demonstrated a lower order of natural and acquired resistance and a higher degree of hypersensitivity to tuberculin in the American Negro.

Certain terms must be defined before Figures 2 and 4 can be understood. The term "relapse" in this study was used to designate those who developed proved tuberculosis subsequent to effusion. Relapse might occur either as a part of progressive disease in which effusion was the initial sign (but without discernible tuberculosis or pulmonary infiltration at the time of effusion) or as an event subsequent to recovery from the initial illness.

The term "well" has been used to include all those who remained asymptomatic during observation and did not develop proved tuberculosis (ignoring the results of bacteriological study of the initial effusion fluid). The well were further categorized according to the appearance of the serial chest x-ray films taken during the follow-up period.

"Well without scar by x-ray" was used to designate those "well" whose chest roentgenograms remained unchanged during observation insofar as the pulmonary parenchyma was concerned. Residua which were definitely pleural were not considered in this part of the study.

"Well with scar by x-ray" sets apart those who remained asymptomatic, without recognized tuberculosis subsequent to their effusions, and exhibited no disease evident in the chest x-ray films until either fibrosis or calcification made it apparent. Most of these appeared as pin-point in size, and in some patients they disappeared before follow-up was terminated.

The category "well with active disease by x-ray" includes those who had no symptom or proved tuberculosis subsequent to effusion, but who developed a radiographically active pulmonary lesion, usually quite small. The mode of life of patients in this group was not modified because of the x-ray film findings. The x-ray disease was either stable, regressive, or gone at the time of last observation. There is no intended implication that the radiographically active disease was necessarily tuberculous. Some of the patients in this category had pulmonary infiltrates which appeared and disappeared within a period of less than two or three months (the interval between chest x-ray films), but many had more persistent findings (e.g., a patient found ultimately to have hemoglobin-C disease).

The dead are subdivided according to the causative importance of tuberculosis. Those who are listed as "dead *from* tuberculosis" died with tuberculosis as the major or sole cause of death. Those tabulated as "dead *with* tuberculosis" were found to have tuberculosis at the time of death, but this disease was not a major cause of death. There was only one patient "dead from other causes." No evidence of tuberculosis was found at autopsy. Death was due to disseminated lupus erythematosus. She is omitted from consideration in Figures 2, 3, and 6.

Since many studies have shown that what we have called "idiopathic serofibrinous pleural effusion" is usually tuberculous, some readers may wish to tabulate the results shown in Figure 4 in a less critical manner.

If the presence of a pulmonary infiltrate which persists for more than several weeks is all that is required for the diagnosis of tuberculosis in the posteffusion state, then the categories "well with scar by x-ray" and "well with active disease by x-ray" can be combined with those containing patients who developed proved tuberculosis. From this maneuver one might conclude that 53 per cent of the antimicrobially treated and 83 per cent of the untreated developed either active clinical tuberculosis or "x-ray pulmonary tuberculosis." This statistical device is of doubtful value in our opinion. Such uncritical grouping might include a significant number of patients with non-tuberculous pulmonary diseases. Of principle interest is the fact that 44 per cent of our treated patients not only remained well but had no evidence of any parenchymal disease by x-ray during follow-up.

Figure 5 tabulates the annual incidence of tuberculosis among the antimicrobially treated and untreated. Over 40 per cent of the control group developed active tuberculosis during the first two years, whereas only 11 per cent of the antimicrobially treated showed definite evidence of the disease during the same interval. A secondary peak of relapse occurs at the fifth year in the untreated group and at the seventh year in the treated group. This secondary peak of relapse gains more importance when one thinks about the percentage of total relapses occurring at any stated interval rather than annual incidence. Only 7 per cent of all relapses among the untreated occurred after year five, whereas 25 per cent of all relapses occurred during year seven for the antimicrobially treated group. This secondary peak of relapse is both greater and later in the antimicrobially treated group, any may indicate that inadequate treatment can prolong the interval between effusion and

ANNUAL INCIDENCE OF TUBERCULOSIS
AMONG ANTIMICROBIALLY TREATED AND UNTREATED GROUPS

Year	Number at risk		Developed Tuberculosis	Died without Tuberculosis	Cases per 100 (%)
1	Treated	45	4		8.89
	Untreated	47	9		19.15
2	Treated	41	1		2.44
	Untreated	38	9		23.68
3	Treated	40	1		2.50
	Untreated	29	3		10.34
4	Treated	39	0	1	0.00
	Untreated	26	2		7.69
5	Treated	37*	0		0.00
	Untreated	24	5		20.83
6+	Treated	33†	2		6.06
	Untreated	19	2		10.53

* One patient lost to follow-up after 4 years.
† Only 33 patients followed for 6 or more years.

FIGURE 5: In the treated group only 75 per cent of the relapses occurred within the first five postpleuritic years whereas 93 per cent of relapses among the untreated took place within this interval.

relapse. This, also, would tie in with the ideas of Pinner and Kasper[1] and Rich[2] of the more rapid decline of acquired resistance in the American Negro. Inadequate treatment may serve to tide over the postpleuritic period of invasion, keeping the disease in check while resistance is acquired. As resistance declines with succeeding years, dormant foci may reactivate.

Because acute tuberculous pleurisy with effusion is, as a rule, a more violent process in the hypersensitive American Negro than among Caucasians, we thought it might be informative to compare the effects of effusion upon the involved extrapulmonary hemithorax in the control and treated groups. Both treated and untreated groups were managed with repeated needle aspirations. Figure 6 tabulates the fate of the extrapulmonary hemithorax with and without antimicrobials. The distribution of large, medium, and small effusions was almost identical in the two groups (Figure 1). Each involved hemithorax was tabulated at the intervals of six months, one year, three years, and five years. Each abnormality present was separately recorded. Consequently, a single hemithorax might present multiple abnormalities. Whenever relapse occurred, the patient was removed from further consideration.

Inspection of Figure 6 makes it clear that the fate of the extrapulmonary hemithorax involved by a serofibrinous pleural effusion is likely to be much improved by antimicrobial therapy. Seventy-four per cent of the hemithoraces under observation at year five in the treated group were normal, whereas only 27 per cent of the untreated fell into the same category. This is a significant difference which might have been greater if treatment had been better. Furthermore, the serious post-

FATE OF THE EXTRAPULMONARY HEMITHORAX WITH AND WITHOUT ANTIMICROBIALS

	Treated				Untreated			
	6 mos.	1 yr.	3 yrs.	5 yrs.	6 mos.	1 yr.	3 yrs.	5 yrs.
Mediastinal shift	0	0	0	0	2	5	3	2
Impaired diaphragm	10	6	3	2	8	10	9	5
Thoracic deformity	0	0	0	0	1	2	3	2
Pleural thickening	13	8	7	4	9	13	7	3
Costophrenic blunting	25	20	11	8	14	21	14	13
Persistent fluid	4	2	0	0	18	8	3	2
Radiographically normal	15	20	29 (67%)	31 (74%)	2	6	7	6 (27%)

FIGURE 6: Each involved hemithorax was classified at six months, one year, three years and five years or until relapse occurred. Does not include patient with disseminated lupus.

pleuritic residuals such as mediastinal shift and thoracic deformity were not present among the treated but were among the untreated.

Some of the data collected during this study was believed to be of insufficient importance to tabulate. Among the less significant findings were the number and sides of recurrent effusion, and the side of disease subsequent to the original effusion.

In the untreated group, there were seven patients who suffered one or more serofibrinous effusions after the initial one. In the antimicrobially treated group, there was only one who developed a second effusion.

The type of postpleuritic tuberculosis which developed in each group is of particular interest. In the untreated group, 76 per cent of the postpleuritic tuberculosis was intrathoracic, and 24 per cent extrathoracic. On the contrary, in the treated group only 25 per cent of the relapses were due to intrathoracic tuberculosis, whereas 75 per cent were extrathoracic. Of the total number of deaths in both groups, 51 per cent were due to miliary or miliary-meningeal disease. This rather grim fact, together with the high incidence of extrathoracic tuberculosis, emphasizes both the frequency of lympho-hematogenous dissemination and the seriousness of serofibrinous effusion in the Negro.

If one subdivides both the control and antimicrobially treated groups into subgroups according to their postpleuritic fate, those findings of minor interest can be summarized in better context. We have attempted to include data of primary interest to the statistically-minded in the following paragraphs.

Those receiving no antimicrobials who died.

Ten patients in the control group died during observation. None was younger than 30 and seven were over 50. One presented with polyserositis and two others had bilateral pleural effusion. Three had only minimal (grade 3) effusion. Two deaths occurred within the first six months after admission to hospital. Neither death was due primarily to tuberculosis. Three deaths were due to miliary or miliary-meningeal tuberculosis.

MORBIDITY AND MORTALITY FROM TUBERCULOSIS IN POSTPLEURITIC CAUCASIANS

AUTHOR AND YEAR	NUMBER OF PATIENTS WITH EFFUSION	PERCENTAGE FOLLOW-UP	DURATION OF FOLLOW-UP	PERCENTAGE DEVELOPING TUBERCULOSIS	PERCENTAGE DYING FROM TUBERCULOSIS
Roper and Waring (1955)	141 (all males)	100	5 or more years	65.2	3.5
Ottle (1950)	78 (all males)	100	5 or more years	51.3	6.4*
Thompson (1946)	190 (107 males)	92.6	1-8 years	25.	3.5
Patiala (1954)	2,816 (all males)	99.8	7-9 years	43.1	15.1

* 6.4% died from tuberculosis. One additional death with tuberculosis (total mortality 7.7%).

Includes 14 patients below age 10 and 39 who were observed only 1 year. Morbidity and mortality calculated by life-table method. Includes 39 patients with x-ray evidence of primary pulmonary tuberculosis.

FIGURE 7: None of the studies listed involve treatment with antimicrobials.

Antimicrobially untreated patients developing non-fatal tuberculosis.

Twelve women and eight men among the control group developed active tuberculosis during postpleuritic follow-up but did not die from their disease. Two relapsed during the first three posteffusion months and one more developed tuberculosis between three and six months after effusion. Eleven of the relapses occurred during the first two years. Four patients relapsed during the fifth year, following which only one non-fatal relapse took place. This patient developed active tuberculosis during the seventh posteffusion year. Two patients in this subdivision of the control group presented with polyserositis. The type of relapse was pulmonary in 13, pleuropulmonary in three, polyserositis with epididymitis in one, pleural and osseous in one, cervical lymph nodes in one, and endobronchial in one.

Those untreated with antimicrobials who did not develop tuberculosis.

There were 17 patients who neither received antimicrobial therapy nor developed diagnosed tuberculosis during five years or more of observation. There was no patient with polyserositis in this group. One of this group probably represented a sulfonamide-treated synpneumonic effusion. One, who is classified in Figure 4 as "well with active disease by x-ray," was particularly interesting. This patient was the only one in this group with bilateral pleural effusion at onset. He had a recurrent effusion on one side four years after his initial illness. During seven years of postpleuritic follow-up he slowly developed bilateral diffuse interstitial infiltration (radiographic "fibrosis"). Bacteriologic diagnosis was attempted unsuccessfully several times. In his seventh year of follow-up he was found to have hemoglobin-C disease. Is it possible that the pulmonary "infiltration" was due to hemosiderosis and the pleural effusions to active episodes of hemoglobin-C disease? Of the entire 17 in this group, five had radiographically active disease at some time during follow-up. Four additional patients developed calcific or fibrotic pulmonary "scars" which were not present prior to effusion.

Antimicrobially treated patients who did not develop tuberculosis.

In this subgroup there were thirty-five patients who were followed for a minimum period of five years after effusion. One patient was lost after four years of follow-up and one died from disseminated lupus erythematosus after fifty-three months of follow-up. There were six patients with polyserositis.

Failure of antimicrobial treatment.

There were two deaths from tuberculosis among the treated group, both due to miliary-meningeal involvement. One had received treatment with streptomycin and paraminosalicylic acid for ten months. The type of non-fatal relapse was pulmonary in two, pelvic in one, pelvic and cervical lymph nodes in one, pleural and osseous in one, and meningeal in one. Only one of the treatment failures presented initially with polyserositis.

Discussion

It seems strange that so little has been written about the place of antimicrobials in the treatment of primary serofibrinous pleural effusion. Perhaps it is because this expression of tuberculosis is so commonly seen and managed by the general practitioner, internist or surgeon without recognition of the usual etiology and prognosis of the illness. It seems to us that it is the responsibility of phthisiologists to impress

the importance of idiopathic pleural effusion upon those most likely to first encounter it.

Equally disturbing has been the attitude of a number of older phthisiologists and internists with whom we have discussed the significance of idiopathic serofibrinous pleural effusion. They recognize the probability of primary serofibrinous pleural effusion being tuberculous, but think of it as an expression of minimal pulmonary tuberculosis. The early recommendation that minimal pulmonary tuberculosis and idiopathic pleural effusion not be treated with antimicrobials apparently led to the belief by many physicians that tuberculous pleural effusion should be considered in the same category with minimal pulmonary tuberculosis. This is obviously an error. The classification "minimal pulmonary tuberculosis" referred to the quantity of pulmonary parenchymal disease present, as estimated from x-ray films, and refers to the character of the disease only to the point of excluding visible cavitation. The disease present could be old or recent, active or inactive. If an idiopathic pleural effusion is due to tuberculosis, it is always due to active, progressive disease. The fact that no parenchymal infiltration may be seen in the chest radiogram is unimportant and quite unrelated to the clinical significance of the process.

When related to the duration of follow-up, the postpleuritic mortality from tuberculosis among the Negroes studied by Bonilla,[3] and Jones and Dooley[4] is not significantly different from that observed by us among the Negroes who did not receive antimicrobials. The mortality from tuberculosis among our "untreated" Negroes is almost identical with that observed by Farber.[5] The most impressive finding of our study, in our opinion, is the fact that the *mortality* among the "untreated" exceeded the *morbidity* among the "treated."

The postpleuritic morbidity from tuberculosis among young, antimicrobially untreated, white men in military service is not greatly dissimilar in the three studies by Roper and Waring,[6] Oille[7] and Pätiälä.[8] The morbidity reported by them is similar to that shown by us for untreated Negroes. The much lower morbidity reported by Thompson[9] among civilians may be due *in part* to the inclusion of 14 children and the short duration of follow-up of many adults.

The mortality from tuberculosis seems to be significantly higher among antimicrobially untreated Negroes with idiopathic pleural effusion than the mortality among similar groups of Caucasians. Emerson[10] attempted to analyze the statistical validity of a great many reports of morbidity and mortality from tuberculosis following primary serofibrinous effusion. Selecting only those studies which he believed to be suitable for statistical conclusions, he found a mean mortality of 7 per cent for those not given "prolonged bed rest" and 4.1 per cent for those given "prolonged bed rest." These percentages are similar to the mortality figures shown in Figure 7 for the studies of Roper and Waring,[6] Oille,[7] and Thompson.[9] The mortality in Pätiälä's series[8] is much higher — almost as high as that for untreated Negroes and the reasons for this discrepancy are not obvious. Differences in war-time conditions among the military in Finland, Canada, and the United States may account for some of the difference.

The difference between the postpleuritic mortality among antimicrobially untreated Caucasians and Negroes is, in our opinion, related to the somewhat different pathogenesis of primary and postprimary tuberculosis in the two races. In the adult Caucasian who has acquired resistance as well as hypersensitivity, there is marked limitation of spread of tubercle bacilli from secondary foci to regional lymph nodes and limitation of successful spread to distant organs.[2] This does not appear to be true of many adult Negroes. Regional lymph node involvement and subsequent widespread hematogenous implantation is often seen in Negroes. Both natural and acquired resistance seems to be of a lower order in this racial group. Accordingly, one would expect to encounter a greater incidence of extrapulmonary tuberculosis and secondary pulmonary dissemination on this basis alone. The post-primary Negro has been shown by Rich[2] and Pinner and Kasper[1] to lose much of his acquired resistance with the passage of time. Such an adult may respond to reinfection tuberculosis in the manner characteristic of the primary stage and serious secondary foci may be established.

Hypersensitivity to tuberculin in the Negro is of a high order. Since hypersensitivity is greater in the adult Negro[2] than in the adult Caucasian, bilateral pleural effusion and polyserositis might occur more frequently in the Negro on this basis alone. It is not necessary to consider all instances of polyserositis as evidence of hematogenous dissemination. Nevertheless, hematogenous spread before and after pleural effusion seems much more common and important in the Negro than in the white. The same can be said for lymphogenous dissemination. Pinner and Kasper[1] demonstrated that lymphatic involvement is more massive, more exudative in the American Negro, and lymphogenous spread after establishment of a definite tuberculous focus much more frequent. This, too, makes bilateral pleural effusion and polyserositis more likely in the Negro.

These principles seem to apply to the distribution of type of relapse in our two groups of Negroes. In the untreated group, postpleuritic relapse was intrathoracic in 76 per cent. The initial pulmonary foci of tuberculosis, being modified by bed rest and host resistance only, progressed to visibility and diagnosibility, and the patient was then classified as having relapsed. This occurred early during postpleuritic observation for the most part. Among the antimicrobially treated group, these initial

pulmonary foci of tuberculosis were suppressed by chemotherapy. Our treatment regimens were inadequate to permanently suppress the distant lymphogenous and hematogenous implants which made themselves known much later in post pleuritic follow-up.

It seems unnecessary to speculate about the results of antimicrobial treatment of idiopathic pleural effusion. If antimicrobial therapy can significantly modify the prognosis and course of active tuberculosis, then postpleuritic morbidity and mortality should be much less following chemotherapy. Our group of antimicrobially treated Negroes fared significantly better than the untreated, particularly with respect to mortality. It is, perhaps, surprising that the treated patients did so well when one considers the inadequacy of the treatment given. Although we started our study with the aim of comparing antimicrobially treated and untreated patients with idiopathic pleural effusion on a random basis, we ended it knowing that our studies showed that a little treatment is better than none.

Although the results of our studies afford no proof, we believe that treatment for idiopathic pleural effusion in the Negro should be tailored to the premise that the patient has miliary tuberculosis. Our total mortality from tuberculosis among the antimicrobially treated was due to miliary-meningeal infection.

It is apparent from the postpleuritic course of those in the untreated group that most of our idiopathic serofibrinous pleural effusions were due to tuberculosis. We do not believe that this high incidence of a single etiologic agent is justification for using any terminology which implies that such an effusion is tuberculous. Disseminated lupus erythematosus, and probably both sulfonamide treatment of a pyogenic synpneumonic effusion, and hemoglobin-C disease were responsible for effusion of a serofibrinous type among our Negro patients. It is rather surprising that none of more than 90 idiopathic pleural effusions were due to neoplasm.

SUMMARY

1. Forty-seven American Negroes with idiopathic pleural effusion were treated with bed rest of variable duration together with therapeutic aspiration. Sixty-four per cent of them developed proved tuberculosis during a minimum follow-up of five years. Twenty-one per cent of them died.

2. During the same period of time and under the same hospital conditions, 45 American Negroes were given chemotherapy, most of which was inadequate by present day standards, and were then followed for a similar period of time. Of this group 17.7 per cent developed postpleuritic tuberculosis, and 4.4 per cent died. Even inadequate antimicrobial therapy was able to alter significantly postpleuritic morbidity and mortality from tuberculosis. The mortality among the untreated group exceeded the morbidity among the treated.

3. Pleural and thoracic complications of serofibrinous effusion were significantly fewer and less severe following antimicrobial therapy.

4. Our data suggest that inadequate antimicrobial therapy may prolong the interval between effusion and relapse in the American Negro.

5. Our studies confirm the findings of others: bilateral pleural effusion, polyserositis, and extrathoracic tuberculosis are more common in the adult American Negro than in the Caucasian.

6. It is our belief that idiopathic pleural effusion in the American Negro is a particularly serious event, and when it is associated with a positive tuberculin reaction, should be treated as miliary tuberculosis.

RESUMEN

1. Cuarenta y siete negros americanos que sufrían de derrame pleural idiopático, se trataron con reposo en cama por tiempo variable así como con aspiración. Sesenta y cuatro por ciento de ellos presentaron tuberculosis demostrada durante un período de observación mínimo de cinco años. Veintiún por ciento de ellos murieron.

2. Durante el mismo período de tiempo y bajo las mismas condiciones hospitalarias, 45 negros americanos se trataron con quimioterapia, en la mayoría de los casos, inadecuada, si se consideran las normas actuales y se observaron por un período de tiempo similar. De este grupo, 17.7 por ciento presentaron tuberculosis postpleurítica y 44 por ciento murieron. Aún la terapéutica antimicrobiana inadecuada fué capaz de alterar de modo significativo la morbilidad postpleurítica por tuberculosis. La mortalidad entre los no tratados, excedió a la morbilidad entre los tratados.

3. Las complicaciones pleurales y torácicas del derrame serofibrinoso fueron significantemente menores y menos graves después de la terapéutica antimicrobiana.

4. Nuestros datos sugieren que la terapéutica antimicrobiana inadecuada, pueden prolongar el intervalo entre derrame y recaída en el negro americano.

5. Nuestros estudios confirman los hallazgos de otros: que el derrame pleural bilateral, la poloserositis, y la tuberculosis extra-pulmonar son más comunes en el aduito negro americano que en el de raza caucásica.

6. Creemos que el derrame pleural idiopático en el negro americano es un acontecimiento particularmente serio y cuando está asociado a una reacción tuberculínica positiva, debe tratarse como tuberculosis miliar.

RESUMÉ

1. 47 Noirs Américains atteints d'épanchement pleural idiopathique furent traités par le repos au lit de durée variable, associé à l'évacuation thérapeutique. 64% d'entre eux développèrent une tuberculose pendant un temps de surveillance d'un minimum de cinq ans. 21% d'entre eux moururent.

2. Pendant la même période de temps et sous les mêmes conditions d'hospitalisation, 45 Noirs Américains furent soumis à la chimiothérapie, la plupart des traitements étaient peu conformes aux standards actuels, les malades suivis pendant une période de temps analogue. Dans ce groupe, 17,7% développèrent une tuberculose post-pleurétique, et 44% d'entre eux moururent. Même une thérapeutique antimicrobienne inadaptée fut capable de modifier d'une façon importante la morbidité post-pleurétique et la mortalité par tuberculose. La mortalité parmi le groupe qui resta sans traitement surpassa la morbidité du groupe traité.

3. Les complications pleurales et thoraciques de l'épanchement séro-fibrineux furent nettement moins nombreuses et moins graves après traitement antimicrobien.

4. Les constatations des auteurs leur donnent à penser que le traitement antimicrobien même mal conduit peut retarder l'intervalle entre l'épanchement et la tuberculose pulmonaire chez le Noir Américain.

5. Ces études confirment les constatations faites par ailleurs: l'épanchement pleural bilatéral, la polysérite et la tuberculose extrathoracique sont plus fréquentes chez l'adulte Noir Américain que chez le Caucasien.

6. Les auteurs pensent que l'épanchement pleural idiopathique chez le Noir Américain est un fait particulièrement grave et qui, lorsqu'il est associé à une réaction tuberculinique positive, devrait être traité comme une tuberculose miliaire.

ZUSAMMENFASSUNG

1. Es wurden 47 amerikanische Neger mit idiopathischem pleuralem Erguss mit Bettruhe von verschiedener Dauer und mit therapeutischenPunktionen behandelt. Bei 64% von ihnen entwickelte sich nachgewiesenermassen eine Tuberkulose im Verlauf einer Mindest-Nachbeobachtungszeit von 5 Jahren. 21% von ihnen verstarben.

2. Zur gleichen Zeit und unter denselben Bedingungen des Krankenhauses erhielten 45 amerikanische Neger eine Chemotherapie, die allerdings nach der heutigen Auffassung in den meisten Fällen nicht adäquad war, und wurden dann während einer ähnlichen Zeitperiode nachbeobachtet. In dieser Gruppe entwickelte sich, bei 17,7% eine postpleuritische Tuberkulose, und 44% verstarben. Es war also selbst eine nicht adaquate antimikrobielle Therapie imstande, die postpleuritische Morbidität und Mortalität an Tuberkulose entscheidend zu beeinflussen. Die Mortalität in der unbehandelten Gruppe übertraf die Morbidität bei der behandelten Gruppe.

3. Die pleuralen und thorakalen Komplikationen bei serofibrinösen Ergüssen waren eindeutig geringer und weniger schwer nach antimikrobieller Therapie.

4. Unsere Erhebungen legen die Vermutung nahe, dass eine nicht adaquate antimikrobielle Therapie imstande ist, das Intervall zwischen Erguss und Rückfall bei den amerikanischen Negern zu verlängern.

5. Unsere Untersuchungen bestätigen die von anderer Seite erhobenen Befunde: Bilateraler, pleuraler Erguss, Polyserositis und extra-thorakale Tuberkulose kommen beim erwachsenen amerikanischen Neger häufiger vor als bei den Kaukasiern.

6. Nach unserer Überzeugung ist der idiopathische pleurale Erguss beim amerikanischen Neger ein besonders ernsthaftes Ereignis, und tritt er in Verbindung mit einer positiven Tuberkulinreaktion auf, so muss man ihn wie eine Miliartuberkulose behandeln.

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The Maximal Expiratory Flow Rate of Normal Individuals*

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While the maximum expiratory flow rate with the rapid kymograph is being increasingly employed as a test for possible intrabronchial obstruction, little data are available on the range of normal in men and women of different ages. It is the purpose of this paper to determine the 200-1200 ml. maximum expiratory flow rate in individuals without recognizable pulmonary disease.

Materials and Methods

A total of 167 individuals was studied which included 85 men and 82 women ranging in age from 20 to 59 years. The criteria for normalcy were based on the following requirements: 1) no history of cardiopulmonary disease, 2) normal chest x-ray film within six months. The total vital capacity was measured with a 6-liter Vitalometer having a 70-centimeter noncorrugated rubber tube with an internal diameter of 2.0 centimeters, and the maximum breathing capacity was measured with a Collins 13.5-liter respirometer having a double 92-centimeter noncorrugated tube with an internal diameter of 3.3 centimeters.

All of the individuals studied were either house staff or employees of the hospital or patients who were ambulatory.

The flow rate was determined on a 6-liter Collins Vitalometer with a direct writing pen inscribing on a Gorell and Gorell monodrum rotating

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TABLE 1 — THE MEAN HEIGHT IN CENTIMETERS, MEAN WEIGHT IN KILOGRAMS, AND MEAN BODY SURFACE AREA IN SQUARE METERS FOR EACH AGE GROUP

MEN

Number of Patients	Age Range	Age Mean	Mean Height	Mean Weight	Mean M^2BS
22	20-29	25.81	175.8	72.68	1.88
20	30-39	33.15	176.1	78.65	1.85
22	40-49	44.95	174.2	76.55	1.92
21	50-59	53.43	171.3	77.38	1.89

TABLE 2 — THE MEAN HEIGHT IN CENTIMETERS, MEAN WEIGHT IN KILOGRAMS, AND MEAN BODY SURFACE AREA IN SQUARE METERS FOR EACH AGE GROUP

WOMEN

Number of Patients	Age Range	Age Mean	Mean Height	Mean Weight	Mean M^2BS
20	20-29	22.80	166.0	58.0	1.65
20	30-39	33.4	163.9	60.8	1.66
20	40-49	44.8	163.1	69.4	1.74
22	50-59	53.7	157.7	64.4	1.65

TABLE 3 — THE MAXIMUM BREATHING CAPACITY IN LITERS/MINUTE AND TOTAL VITAL CAPACITY IN LITERS FOR MEN IN EACH AGE GROUP

Age Range	Maximum Breathing Capacity		Total Vital Capacity	
	Range	Mean	Range	Mean
20-29	125-300	186	3.80 - 5.40	4.73
30-39	138-250	176	3.35 - 5.10	4.45
40-49	135-232	171	3.65 - 5.30	4.28
50-59	128-175	150	3.15 - 4.80	3.86

TABLE 4 — THE MAXIMUM BREATHING CAPACITY IN LITERS/MINUTE AND TOTAL VITAL CAPACITY IN LITERS FOR WOMEN IN EACH AGE GROUP

Age Range	Maximum Breathing Capacity		Total Vital Capacity	
	Range	Mean	Range	Mean
20-29	110-169	138	3.0 - 4.4	3.54
30-39	100-156	127	2.6 - 4.0	3.28
40-49	94-138	117	2.5 - 3.65	3.02
50-59	80-144	107	2.06 - 3.5	2.74

TABLE 5 — THE TIMED VITAL CAPACITY RANGES AND MEANS FOR MEN EXPRESSED IN PER CENT FOR EACH AGE GROUP

	Timed Vital Capacity (c.c.)					
	0.5 sec.		1.0 sec.		3.0 sec.	
Age	Range	Mean	Range	Mean	Range	Mean
20-29	54-80	64.8	77-100	86.1	97-100	99
30-39	53-78	67.9	71-94	85.3	92-100	99
40-49	44-78	67.1	75-93	83.9	95-100	99
50-59	53-77	66.5	75-98	83.0	94-100	99

TABLE 6 — THE TIMED VITAL CAPACITY RANGES AND MEANS FOR WOMEN EXPRESSED IN PER CENT FOR EACH AGE GROUP

	Timed Vital Capacity (c.c.)					
	0.5 sec.		1.0 sec.		3.0 sec.	
Age	Range	Mean	Range	Mean	Range	Mean
20-29	57-85	67.0	77-93	87.2	100	100
30-39	52-80	65.4	76-100	85.2	100	100
40-49	50-74	63.6	71-87	81.4	95-100	99
50-59	55-74	65.2	68-87	80.1	92-100	99

TABLE 7 — 200 — 1200 CC. MAXIMUM EXPIRATORY FLOW RATE IN MEN EXPRESSED IN LITERS/SECOND WITH RANGE, MEAN, AND THE LOWER LIMIT OF NORMAL FOR EACH AGE GROUP.

Age	Range	Mean and S. D.	Lower Limit of Normal
20-29	6.8 - 11.9	9.5 ± 1.1	7.3
30-39	7.3 - 11.9	9.6 ± 1.3	7.0
40-49	5.3 - 11.9	8.7 ± 1.2	6.3
50-59	5.6 - 11.8	8.4 ± 1.2	6.0

TABLE 8 — 200 — 1200 CC. MAXIMUM EXPIRATORY FLOW RATE IN WOMEN EXPRESSED IN LITERS/SECOND WITH RANGE, MEAN, AND THE LOWER LIMIT OF NORMAL FOR EACH AGE GROUP.

Age	Range	Mean and S. D.	Lower Limit of Normal
20-29	5.3 - 7.3	6.5 ± 0.8	4.9
30-39	4.1 - 8.6	6.2 ± 0.96	4.3
40-49	3.8 - 7.9	5.5 ± 0.93	3.6
50-59	3.4 - 7.9	5.1 ± 0.94	3.2

at a speed of 94.9 mm. per second. The subjects were instructed to perform a maximum rapid expiration. All tests were done in the standing position. A minimum of three determinations was done so that at least two checked within 0.5 liter per second. The 200-1200 ml. portion of the expirogram was measured and the flow rate was determined according to the method of Cander and Comroe,[1] and interpreted to read in liters per second.

Results

The results are summarized in Tables 1 to 8. The maximum expiratory flow rate range was rather wide, varying from 5.3 to 11.9 liters per sec. in men and from 3.4 to 8.6 liters per sec. in women. There was a slight decrease in flow rate with increasing age in both sexes. Two standard deviations encompassed 97.5 per cent of the patients. The "lower limit of normal" was considered to be two standard deviations below the mean.

Discussion

An effort was made to correlate the maximum expiratory flow rate with various physical factors other than age and sex, i.e., height, weight, body surface area. However, no significant correlation was found. It was of interest that the maximum expiratory flow rate in women was about 60 per cent that of men; this correlates well with the observed maximum breathing capacity. Whether this is truly a sex difference or rather a difference in size of the individuals was not determined.

The observed maximum breathing capacities were generally higher than the predicted values. Several performances were remarkable, achieving total volumes over 250 liters.

The large majority of subjects expired over 60 per cent of the total vital capacity in the first 0.5 second, only one subject failing to reach 50 per cent. The 1.0 and 3.0 second timed vital capacities were in close agreement with the 83 per cent and 97 per cent values reported by Gaensler.[2]

SUMMARY

The maximum expiratory flow rate in liters per second was determined in 85 normal men and 82 normal women who varied in age between 20 and 59 years. The lower limits of normal of this test was defined and determined for each decade and sex studied. The maximum expiratory flow rate in women was about 60 per cent of that found in men, a finding similar to that for the maximum breathing capacity.

RESUMEN

El volumen expiratorio máximo por segundo, se determinó en 85 hombres normales y en 82 mujeres normales, que variaron desde 20 a 59 años de edad.

Los límites más bajos de lo normal de esta prueba, se definieron y se determinaron para cada década de la vida, así como para cada sexo.

El volumen expiratorio máximo en las mujeres, fué como el 60 por ciento del encontrado en los hombres, hallazgo que fué similar para la capacidad respiratoria máxima.

RESUMÉ

Le débit expiratoire maximum en litres seconde fut déterminé chez 85 hommes normaux et 82 femmes normales, dont les âges variaient entre 20 et 59 ans. Les limites inférieures normales de ce test furent définies et déterminées pour chaque décade et sexe étudiés. Le débit expiratoire maximum chez les femmes fut de 60% de celui trouvé pour les hommes, constatation semblable à celles trouvés pour la capacité respiratoire maximale.

ZUSAMMENFASSUNG

Es wurde die maximale Ausatmungsluft in Litern pro Sekunde bei 85 gesunden Männern und bei 82 gesunden Frauen bestimmt, deren Alter zwischen 20 und 59 Jahren lag. Die unteren Grenzen des Normalen wurden für diesen Test ermittelt und für jede untersuchte Lebensdekade und Geschlecht bestimmt. Die maximale Ausatmungsluft betrug bei Frauen etwa 60% der bei Männern gefundenen Werte, ein Ergebnis, ähnlich demjenigen für den Atemgrenzwert.

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Isoniazid Therapy of Primary Tuberculosis in Children

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There are millions of children in the world today who have been infected by tubercle bacilli. These children will be a significant source of active tuberculosis of tomorrow. With the advent of a potent antituberculosis drug such as isoniazid (INH), a major attack on this disease must be directed to primary tuberculosis in children.[1-4]

This paper is a report on a study of 128 children under 36 months of age with positive tuberculin reactions who have been under the care of this service for 12 to 36 months. These young children were selected for evaluation of INH therapy because of the high morbidity and mortality rates of primary tuberculosis at this age period.[5-7] The severity of primary infection in this series of cases is indicated by the fact that almost one-half of the patients had already developed manifested forms of active tuberculosis when first seen and that tubercle bacilli were demonstrated in 45 of the 128 cases. The age distribution is shown in Table 1.

Drug therapy consisted of INH and PAS. The dosage of INH was 5 to 10 mg. per kg. of body weight before 1956. Since 1956, the dosage has been raised to 10 to 15 mg. per kg. For miliary disease and meningitis a higher dosage of 20 to 30 mg. per kg. has been used and streptomycin has been given in addition. PAS in the dosage of 200 mg. per kg. has been given as an adjuvant in all cases. Twelve months of continuous drug therapy was considered minimal for the treatment of tuberculosis. Many patients were given longer periods of therapy because of the extent of the disease. Twelve children received for only short periods of time treatment due to lack of cooperation on the part of the parents — Table 2.

Table 3 shows the types of cases and the results of therapy. There were 66 children with normal chest radiographs. None of these children has developed manifested forms of active tuberculosis to date. Forty-two children had segmental or lobar involvement and five had large mediastinal nodes. These types of cases are much more liable to develop tuberculosis at new sites of the body than those with normal chest radiographs.[8] However, with therapy none has developed tuberculous complications after 12 to 36 months of follow-up observation. Since the great majority of tuberculous complications occur within one year of the primary infection,[6,9] these results indicate that INH therapy is effective in preventing them. This is particularly remarkable in view of the young age and the heavy household contamination of these children. The four patients with miliary tuberculosis recovered uneventfully. None has developed bone or renal tuberculosis. The four cases with meningitis survived, two of whom suffered from mild mental retardation.

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TABLE 1

AGE OF CHILDREN

0 - 12 MONTHS OLD —— 42 CASES
13 - 24 MONTHS OLD —— 56 CASES
25 - 36 MONTHS OLD —— 30 CASES

Since the advent of INH, its therapeutic value in primary tuberculosis in children has been studied by prominent investigators in France, Germany, and Greece. In the United States a large-scale controlled study, including the use of placebo, has been conducted under the auspices of the Public Health Service beginning in 1955 with 32 pediatric clinics participating.[5] The observation so far has shown that 80 per cent of the immediate complications of primary tuberculosis can be prevented by INH therapy even at a small dosage of 4 to 6 mg. per kg. a day.

Witte, in his review of 1220 cases of tuberculosis in infants under one year of age, has shown that INH is effective in the prevention of serious complications of primary tuberculosis especially hematogenous disseminations, which usually result in tuberculous meningitis, miliary tuberculosis, and other extra-pulmonary tuberculosis. For the treatment of infants found with generalized tuberculosis upon admission to the hospital, INH has proved more potent than other anti-tuberculosis drugs.

TABLE 2

DURATION OF THERAPY

MONTHS OF THERAPY	Below 8	8 - 11	12 - 18	19 - 24	25 - 36
NUMBER OF CASES	3	9	79	34	14

114 CHILDREN WERE GIVEN MEDICINE REGULARLY.

14 CHILDREN WERE GIVEN MEDICINE MOST OF THE TIME

Since effective therapy for primary tuberculosis is now available, it is more than ever regrettable that children today develop the more serious forms of tuberculosis. In many countries today, primary tuberculosis is still prevalent. Even in countries where BCG vaccination is used, many children are still found with positive tuberculin reactions who have never been vaccinated with BCG. In some areas, as many as 50 per cent of the children have been infected as shown by positive tuberculin reactions. The infection is often so severe that many become sick and die. Prevention of serious tuberculous diseases by institution of INH therapy during the early stage of primary infection is a crying need of these children and, therefore, a new responsibility of the physicians. The prevalence and severity of primary tuberculosis in those areas offer the physicians excellent opportunities to further the study of the problems relative to drug therapy of primary tuberculosis.

In countries where the incidence of tuberculosis is low and where BCG vaccination is not in general use, a diligent search for primary tuberculosis by tuberculin testing among the young children is an important strategy in tuberculosis control. In Houston, Texas, even in the poorest districts of the city, the tuberculin index is only 1.3 per cent in the pre-school children. The infection rate is even lower in the general children population. The scarcity of tuberculin reactors in the young children makes them sensitive indicators of the hidden pools of tuberculosis in the community. In this series of cases 83 of the 128 children were from homes in which one or more adults were found to have active pulmonary tuberculosis. In 14 cases active tuberculosis was found among the children's close associates outside the home. Therefore, the finding of these infected children is necessary not only for the early treatment, but also for the detection of unrecognized cases of adult tuberculosis in all associated families.

TABLE 3

RESULT OF THERAPY

TYPE OF CASES	NO. OF CASES	LATEST EXAMINATION	NON-PULM. COMPLICATIONS
NO X-RAY EVIDENCE	66	20 HILAR CALC. 46 NORMAL LUNGS	0
LARGE MEDIASTINAL NODES	5	5 RESOLUTION (3 HILAR CALC.)	0
SEGMENTAL OR LOBAR	42	35 RESOLUTION (11 HILAR CALC.) 7 CONTRACTED SEGMENTS	0
PLEURISY	1	1 RESOLUTION	0
PERIPHERAL LYMPHADENITIS	6	4 BIOPSY EXCISION 2 RESOLUTION	0
MILIARY	4	3 RESOLUTION (1 HILAR CALC.) 1 CONTRACTED SEGMENT	0
MENINGITIS	4	2 NO RESIDUAL 2 MENTALLY RETARDED	0

Even in communities of low tuberculosis rate, children from tuberculosis homes run great risk of infection. In our experience as high as 70 per cent of them show positive tuberculin reactions. Many of these infected children do not show signs of illness until in the late stage of the disease. In this series of cases fully one-half of those who were found to have large areas of opacity in the chest radiograph had shown no outward sign of ill health. For this reason all children who have been in close contact with a tuberculous adult must be tuberculin tested for the detection of primary tuberculosis. Since it takes several weeks for the tuberculin sensitivity to develop, the negative reactors must be retested within two to three months for conversion of the tuberculin reaction. In our experience periodic tuberculin testing of known contacts is one of the best ways of finding primary tuberculosis in its early stage when INH therapy would do the most good.

For the millions of children who have been infected by tubercle bacilli a new hope is found in isoniazid.

SUMMARY

1. Isoniazid is effective in preventing tuberculous complications, thus minimizing the danger of primary tuberculosis.

2. Isoniazid is a remarkably effective agent for the treatment of all clinical forms of tuberculosis in children.

3. Since effective therapy is now available, every effort should be made to seek out the infected children by routine tuberculin testing so that they may receive the benefit of INH therapy in the early stage of the infection. Special attention should be given to children under 36 months of age because of the high mortality and morbidity rates of tuberculosis at this age period.

4. In countries where tuberculosis incidence is low and where BCG vaccine is not in general use, routine tuberculin testing of young children serves the dual-purpose of early treatment of primary tuberculosis in children and the detection of unrecognized tuberculosis in adults.

RESUMEN

1. La isoniacida es efectiva para prevenir las complicaciones tuberculosas haciendo así mínimo el peligro de la tuberculosis primaria.

2. La isoniacida es un medicamento notablemente eficaz en el tratamiento de todas las formas de la tuberculosis infantil.

3. Puesto que ahora contamos con un tratamiento efectivo, hay que hacer toda clase de esfuerzos para encontrar los niños infectados, usando para ello la tuberculinorreacción a fin de que reciban pronto los beneficios de la INAH al principio de la enfermedad.

Debe darse especial atención a los niños menores de 36 meses debido a la elevada mortalidad de la tuberculosis en esa edad.

4. En los países donde la tuberculosis es poco frequente y donde la vacuna B.C.G. no es de uso general la prueba de tuberculina, las reacciones tuberculínicas de rutina sirven para el doble propósito de tratar tempranamente la tuberculosis primaria en los niños y para reconocer la tuberculosis ignorada entre los adultos.

RESUMÉ

1. L'isoniazide est efficace pour prévenir les complications tuberculeuses et minimiser ainsi le danger de la tuberculose primaire.

2. L'isoniazide est un produit remarquablement efficace pour le traitement de toutes les formes cliniques de tuberculose chez l'enfant.

3. Puisque nous avons maintenant à notre disposition une thérapeutique efficace, nous devrions faire des efforts pour rechercher les enfants infectés, par les tests courants à la tuberculine, de façon à ce qu'ils puissent recevoir le bénéfice du traitement par l'isoniazide dans le stade précoce de l'infection. Une attention particulière devrait être donnée aux enfants âgés de moins de 36 mois à cause des taux élevés de mortalité et de morbidité par tuberculose à cet âge.

4. Dans les pays où la tuberculose n'a qu'une basse fréquence et où le vaccin B.C.G. n'est pas entré dans la pratique courante, le contrôle tuberculinique systématique des jeunes satisfait le double dessein du traitement précoce de la tuberculose primaire chez les enfants et de la détection de la tuberculose ignorée chez les adultes.

ZUSAMMENFASSUNG

1. Isoniazid ist wirksam hinsichtlich der Verhütung tuberkulöser Komplikationen und setzt die Gefahr der Primärtuberkulose auf ein Minimum herab.

2. Isoniazid ist eine bemerkenswert wirksame Substanz zur Behandlung aller klinischen Formen der Kindertuberkulose.

3. Seitdem nun eine wirksame Therapie zur Verfügung steht, müssen alle Anstrengungen unternommen werden, die infizierten Kindern durch routinemässige Tuberkulinproben herauszufinden, damit sie von der Isoniazid-Therapie Nutzen ziehen schon im Früh-Stadium der Infektion. Besondere Aufmerksamkeit muss man dabei den Kleinkindern unter 3 Jahren widmen in Anbetracht der hohen Mortalität-und Morbiditätsziffern an Tuberkulose in dieser Altersstufe.

4. In Kändern mit geringer Tuberkulose-Häufigkeit und in denen die BCG-Impfung nicht generell angewandt wird, dient die routinemässige Tuberkulinprobe der Kleinkinder dem doppelten Zweck der Frühbehandlung der Primärtuberkulose bei Kindern und der Auffindung unerkannter Tuberkulosefälle bei Erwachsenen.

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Strangulated Diaphragmatic Hernia with Gangrene and Perforation of the Stomach*

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Incarceration of stomach in a diaphragmatic hernia with or without simultaneous inclusion of bowel usually signals a surgical emergency. Symptoms of pain, vomiting and occasionally bleeding, together with roentgenographic studies should lead to easy recognition and appropriate surgical therapy. Rarely, strangulation occurs early; then the above symptoms may be overshadowed by the rapid onset of shock.

Incarceration with acute gastric dilatation may produce serious derangement of cardiopulmonary physiology. The superficial resemblance of the clinical and roentgenographic findings to tension pneumothorax may lead the unwary surgeon to institute improper therapy. The correct diagnosis, if suspected, can almost always be readily confirmed roentgenographically after the passage of a stiff stomach tube with or without the instillation of barium. After preliminary decompression of the stomach in this manner, immediate thoracotomy should be performed to complete the relief of respiratory and circulatory embarrassment and to avert the onset of strangulation with possible gangrene and rupture of the stomach.

Incarceration

The following two case reports illustrate the clinical picture of incarcerated stomach with acute gastric dilatation.

CASE 1: A 22 year old colored man was admitted on transfer to McGuire Veterans Hospital on October 31, 1955 on the Orthopedic Service. Four days previously he had sustained a fractured odontoid process and a steering wheel injury to the chest with fractures of the sixth and seventh left ribs. The head was suspended in traction.

On admission the blood pressure was 150/90, pulse 90, respirations 22. The left chest expanded poorly and was hyperresonant. The heart and trachea were shifted to the right. Breath sounds were absent over the left side of the chest; an occasional tinkle could be heard. The clinical findings together with the appearance of the chest roentgenogram suggested a tension pneumothorax to the examining physician (Figure 1). Accordingly, a No. 16 catheter was inserted through a trocar into the second intercostal space anteriorly. A large amount of air and approximately 300 cubic centimeters of greenish fluid escaped, which was identified as gastric contents. After passage of a Levine tube and injection of lipiodol it was recognized that the stomach was present above the diaphragm. The suspicion of a ruptured diaphragm with incarcerated, dilated stomach was immediately confirmed. Thoracotomy was delayed because of the odontoid fracture. Barium studies showed that neither small nor large bowel was contained in the hernia. Drainage from the intercostal tube ceased within a week and the tube was subsequently removed. The patient was able to take a satisfactory oral diet. He suffered one subsequent period of temporary obstruction of the intrathoracic stomach which was relieved by Levine tube. Repair of the diaphragmatic hernia was performed on March 30, 1956 at which time almost the entire stomach with omentum was found in the left pleural space. No scar could be found on the gastric wall to indicate the site of previous intubation. The diaphragm had ruptured from the dome through into the hiatal orifice. Repair was easily accomplished and convalescence proceeded without complication.

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In this case tension pneumothorax was erroneously assumed to have resulted from the fractured ribs and cursory examination of the chest roentgenogram did, indeed, suggest this. Subsequent review of the film, however, revealed the absence of lung collapsed against the mediastinum and the presence of lung compressed into the apex of the left hemithorax. Whenever these findings are encountered a Levine tube should be inserted to localize the stomach. Under usual circumstances immediate or early

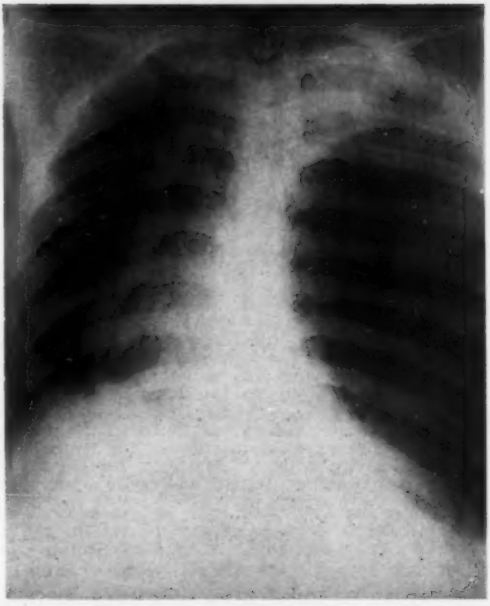
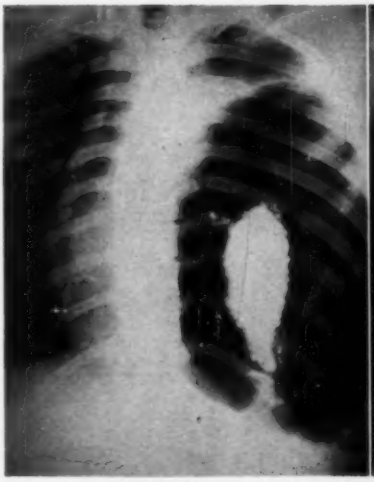


FIGURE 1 (Case 1): Chest film shows large air space (dilated stomach) in left hemithorax with lung compressed into the apex and mediastinum shifted far to the right.



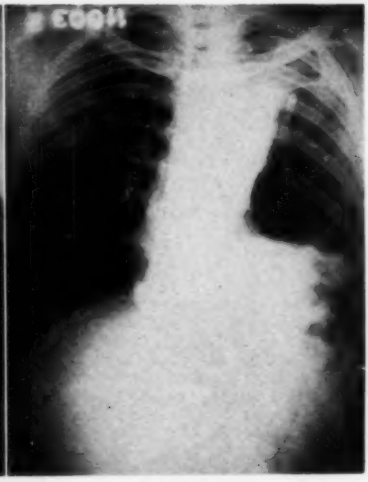


FIGURE 2 FIGURE 3

FIGURE 2 (Case 2): Acute dilatation in incarcerated gastric hernia identified by lipiodol swallow. FIGURE 3 (Case 2): Partial relief of cardiopulmonary derangement by Devine tube intubation.

surgery should be performed, but in this instance decompression of the stomach by an unorthodox route averted any serious complication and obstruction of the stomach was temporarily relieved.

CASE 2: A 37 year old colored man received a knife wound of the mid-axillary portion of the left lower thorax and a laceration of the occipital scalp on September 3, 1955.

During October 1955 he was troubled by intermittent episodes of cramping, epigastric pain, nausea and vomiting. He was thought to have a peptic ulcer, and a bland diet and various medications were prescribed. He did not follow his physician's advice to have a barium study of the gastrointestinal tract.

On October 31, 1955 he experienced a severe episode of cramping, epigastric pain, nausea and vomiting. On the following day he developed severe dyspnea and a mild, intermittent, non-productive cough; he sought admission to St. Philip Hospital.

Physical examination revealed a blood pressure of 100 systolic, pulse 120, respirations 22, temperature 98.6° F. He was in acute distress, with labored respirations and mild intermittent cough. The trachea was deviated slightly to the right. The entire left chest, particularly the left lower portion, exhibited hyperresonance and decreased breath sounds. There were scattered rhonchi and wheezes in the left upper lung field. The right lung was clear. The apical cardiac impulse was displaced toward the right. There was voluntary spasm of the abdomen without tenderness, particularly in the left upper quadrant. Bowel sounds were hypoactive and were not audible over the left thorax.

A roentgenogram showed air in the left lower chest with compression of the left lung into the apex. The mediastinum and heart were shifted markedly to the right. A lipiodol swallow demonstrated that the air space represented dilated stomach extending into the left hemithorax to the level of the third rib posteriorly (Figure 2).

Attempts to pass a standard Levine tube into the stomach for deflation were not successful because of obstruction at the cardia, but a Devine tube was finally passed and the stomach partially decompressed (Figure 3).

At thoracotomy a six centimeter defect was found in the left lateral diaphragm. Most of the stomach and a considerable portion of the transverse colon were herniated into the left pleural cavity through this defect. Neither the stomach nor colon showed any evidence of strangulation. Repair was easily achieved and recovery took place uneventfully.

Strangulation

Of far more serious import are those cases of incarcerated gastric hernia which proceed to strangulation. We have observed two cases of strangulated stomach with rupture which presented many puzzling features and which are reported here for the first time.

CASE 3: A 33 year old colored woman was admitted to St. Philip Hospital on September 18, 1946. Hysterectomy for uterine fibrosis was advised. For two years she had complained of a dull, dragging sensation in the lower abdomen and pelvic region. A history of vague epigastric pain was also obtained. Nine years previously laparotomy with bilateral salpingectomy had been performed for ruptured ectopic pregnancy.

The general physical examination prior to surgery showed nothing abnormal except a systolic murmur at the apex.

Total hysterectomy and appendectomy were performed on September 20. Postoperatively she experienced some nausea and vomiting and complained of a moderate degree of abdominal pain. Her condition, however, remained satisfactory until the third postoperative evening when she was found in a state of profound shock. The blood pressure was unobtainable and her pulse was rapid and feeble. Breath sounds were absent over the left side of the chest and the percussion note was tympanitic anteriorly and dull posteriorly. A roentgenogram of the chest made with the patient in the supine position revealed the heart and mediastinum displaced markedly to the right with a diffuse haziness over the entire left side of the thorax (Figure 4). A small air pocket overlay the central portion of the left side of the chest. The left diaphragm was not clearly outlined but appeared to be depressed. A consultant suggested the possibility of a spontaneous hemopneumothorax. Aspiration of the left side of the chest yielded 200 cubic centimeters of air and 800 cubic centimeters of a reddish brown, clear, nonodorous fluid. A smear of this fluid was negative, but cultures grew out staphylococcus aureus, alpha hemolytic streptococcus and diphtheroids. The acidity of the fluid was not determined. Transfusions of 500 cubic centimeters of blood and 500 cubic centimeters of plasma sufficed to correct the hypotension.

During the succeeding days she remained critically ill and exhibited signs of extreme toxicity with the pulse ranging around 140. The temperature varied between 100 and 102 degrees. The white blood count rose steeply to 30,000. On the fifth day after the acute episode the patient appeared icteric and the icteric index was found to be 55. The liver was percussed four fingerbreadths below the costal margin.

Daily aspirations of the empyema yielded varying quantities of a brownish-yellow, foul-smelling fluid up to 1000 cubic centimeters, always with some air. One week after the acute episode intercostal catheter drainage was instituted. At this time a consultant postulated the presence of a strangulated diaphragmatic hernia and suggested a barium swallow to demonstrate a gastropleural fistula. Unfortunately the barium failed to enter the pleural cavity and the radiologist reported that the stomach was beneath the diaphragm. Her condition deteriorated rapidly with serum nonprotein nitrogen rising to 336. Shortly before death, lipiodol administered to the patient in the Trendelenburg position passed into the stomach and pleural cavity (Figure 5).

Postmortem examination* revealed the fundus of the stomach with most of the greater curvature and six centimeters of the splenic flexure of the colon herniated through a three centimeter defect in the tendinous portion of the left diaphragmatic leaflet, seven centimeters lateral to the esophageal hiatus. We have classified this as a Foramen of Bochdalek hernia. The wall of the herniated colon was intact but there was a four centimeter perforation at the apex of the fundus of the stomach with black gastric mucosa presenting (Figure 6). The left lung was collapsed. Microscopic study showed that the stomach wall and colon were covered by a definite membrane consisting of both diaphragmatic pleura and peritoneum and identifiable as hernia sac.

CASE 4: A 19 year old white man was admitted to the Mississippi State Sanatorium December 30, 1950. While playing basketball two months previously he had received a blow in the left side. The resulting pain gradually subsided during the next two weeks. On December 18 he developed a lower respiratory infection with fever, cough and hemoptysis. On December 25 he began to have pain in his left posterior chest which radiated to the epigastrium. Pain, gaseous distention, dyspnea and vomiting followed. A chest x-ray film on December 28 showed collapsed left lung with tension pneumothorax. Several thoracenteses yielded large quantities of air and serosanguineous fluid. On December 30 the pain below the rib margin increased and he went into shock.

On admission to the hospital examination revealed a thin, dehydrated, semicomatose man in critical condition with a temperature of 101.6° F, respirations 36, blood pressure 110/90. The left side of the chest was tympanitic and breath sounds were absent. The trachea and heart were shifted to the right. The abdomen was distended, tympanitic and tender throughout with no audible peristalsis. On admission the white blood count was 8,900 and this rose rapidly to 48,000. A catheter was inserted into the second anterior interspace for deflation of the pneumothorax. A

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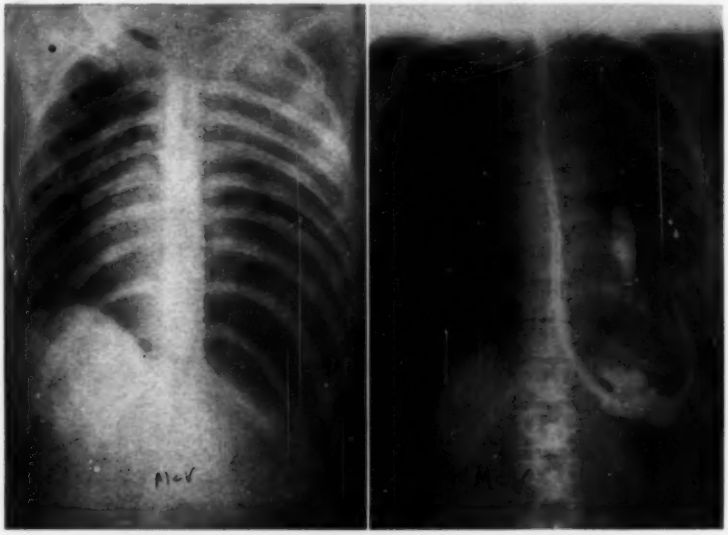

FIGURE 4 FIGURE 5

FIGURE 4 (Case 3): Portable chest film with patient in supine position shows diffuse haziness of entire left thorax with a small air pocket centrally located. Heart displaced to right. FIGURE 5 (Case 3): Demonstration of gastropleural fistula by lipiodol.

Levine tube was passed into the stomach but the patient continued to vomit small amounts of fluid. During the next 72 hours he received over 15,000 cubic centimeters of fluid including three pints of blood.

Chest x-ray films on January 2, 1951 showed that the lungs were somewhat better expanded although dense shadows persisted in the lower chest. Fluid aspirated from the chest at this time contained 10 degrees of total acid while that from the gastric tube contained 8 degrees. Lipiodol studies identified the stomach above the diaphragm and disclosed the intercostal tube in communication with the pneumothorax cavity.

His condition gradually improved. However, on January 8 the Wagensteen apparatus for gastric suction was inadvertently reversed forcing a large quantity of air into the stomach. He immediately complained of severe abdominal pain. Immediate thoracotomy* revealed an 8 centimeter rent through the dome of the diaphragm through which omentum, spleen and dilated stomach had herniated. After the lower lobe of the lung had been dissected free and large amounts of thick fibrinous exudate removed, two large holes were found in the anterior wall of the stomach measuring approximately 2 by 1.5 centimeters and 1 centimeter in diameter respectively. A third, larger hole near the cardioesophageal junction was apparently due to pressure necrosis from the acute angulation against the edge of the intact hiatus. The gangrenous portions were excised and the rents closed. The intrathoracic mass was reduced with difficulty even after enlarging the diaphragmatic rent. The diaphragm was then repaired. Because of his condition no attempt was made at this time to decorticate the lung.

The patient's condition remained critical with persisting peritonitis and empyema and with a bronchopleural fistula. On January 20, 1951 a Stamm gastrostomy was performed and a feeding tube passed through the pylorus into the duodenum. After three weeks he began taking fluids orally which initiated drainage through his thoracotomy tube. Methylene blue confirmed the presence of a cardioesophageal fistula which closed prior to his discharge on June 27, 1951. At that time a drainage tube remained in the empyema cavity.

Ultimately, on November 17, 1953, a Schede thoracoplasty was required to close the bronchopleural fistula.

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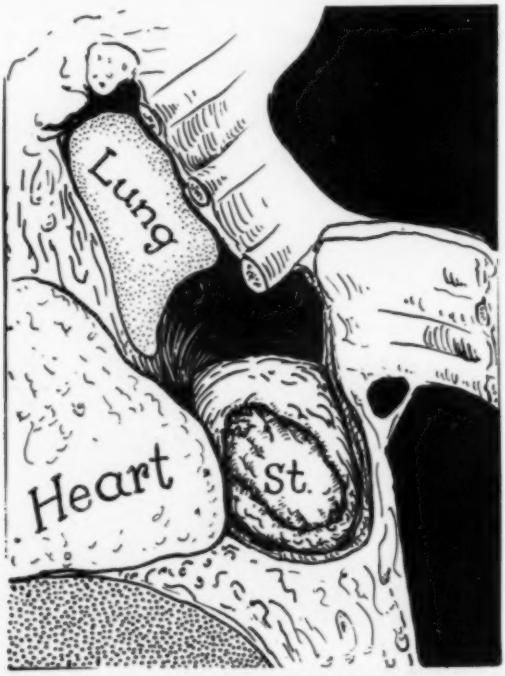

FIGURE 6 (Case 3): Four centimeter perforation in fundus of strangulated stomach. Lung collapsed.

This case illustrates again the error of confusing a dilated stomach with tension pneumothorax. The hernia which did not have a sac and was thought to be traumatic, probably resulted from the basketball injury two months prior to the onset of acute symptoms. Coughing from the respiratory infection may have increased the incarceration to the point of obstruction. It is likely that the perforation at the cardioesophageal junction had occurred just prior to admission, resulting in generalized peritonitis. Bernatz,[18] in reporting the experience from the Mayo Clinic mentions having seen perforation of the esophagogastric junction "where the stomach turned abruptly around an intact esophageal hiatus into the thorax." The perforation in the upper stomach also must have occurred during the early period, only to be sealed off by the adherent lung, until the episode of forced overinflation.

In 1948 Harrington[1] wrote, "I have never seen a stomach which was strangulated as a result of hernia, nor do I believe that it is possible because of the powerful musculature and rich blood supply in the gastric wall." However, a number of surgeons have reported finding congestion, edema and discoloration in the wall of a stomach incarcerated in a diaphragmatic hernia. This may proceed to complete loss of viability as attested to by 17 previous cases of gangrene or perforation of the herniated stomach observed at surgery or autopsy.[2-17]

A review of these cases together with our own has yielded the following information. In 10 of the 19 cases the diaphragmatic hernia was traumatic in origin. In the nine nontraumatic cases the herniation was parahiatal in five, hiatal in two, and through a Foramen of Bochdalek defect in two. Only two were through the right leaf of the diaphragm. The two which we have classified as hiatal are probably a combination of parahiatal and hiatal since almost the entire stomach was herniated through the opening. Nonstrangulated large and small bowel in one case and large bowel in a second case were present in the hernia together with strangulated stomach. In 10 cases thoracentesis had been performed prior to surgery and in all of these sanguineous fluid was obtained. In several the fluid was recognized as gastric and wastested for acidity.

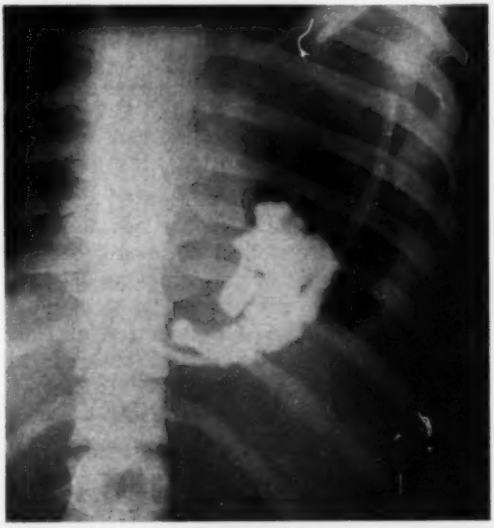

FIGURE 7 (Case 4): X-ray made January 2, 1950 demonstrating tube and injected lipiodol in supradiaphragmatic stomach. Note the thoracotomy tube which is in the free pleural cavity superiorly.

In others the fluid may have represented sanguineous pleural fluid.
the fluid may have represented sanguineous pleural fluid.

In at least six of the 19 cases gangrene occurred within 48 hours or less from the time of onset of symptoms. In other patients a number of days elapsed before surgery was undertaken so the rapidity with which gangrene developed is not known. In four instances the diagnosis was not even suspected until thoracotomy. In five the diagnosis was first determined at autopsy. Of 14 which were operated upon with resection of part or all of the stomach seven died and seven recovered.

In a review of 150 cases of volvulus of the stomach, most of which were unassociated with diaphragmatic hernia, Dalgaard[11] found 15 cases of perforation or gangrene at surgery or autopsy. However, in the cases of gangrene of the stomach occurring as a direct result of diaphragmatic herniation which we have reviewed no case of frank volvulus was found. However, minor degrees of torsion can certainly not be ruled out, particularly in those hernias of the parahiatal type.

Incarcerated diaphragmatic hernias proceeding to strangulation have been reported during pregnancy or labor or have resulted from other causes of increased abdominal pressure, such as vomiting, physical exertion, overeating and postoperative distention. Possible etiologic factors in our case 3 were: the steep Trendelenburg position employed during surgery and increased intraabdominal pressure resulting from postoperative vomiting and ileus. Pain was absent as an important symptom although it may have been somewhat overlooked in the postoperative period. The profound state of shock which this patient exhibited signaled the rapid onset of strangulation. The correct diagnosis might have been entertained if a roentgenogram could have been made with the patient in the upright position. The hemorrhagic fluid aspirated from the chest was not tested for acid but in retrospect suggested gastric contents. A virulent empyema developed after perforation of the stomach, which caused a toxic nephritis, and after drainage of the empyema a large volume of intestinal juices was lost through the thoracogastric fistula. Failure to confirm radiologically the subsequent suspicion of perforated diaphragmatic hernia led to further costly delay.

Symptoms to be expected with strangulated gastric hernia include those seen in acute incarceration with the addition of circulatory collapse. Usually there is a sudden onset of severe pain in the left upper quadrant, epigastrium or lower left chest regions. Vomiting often occurs but is ineffectual and usually without evidence of blood, even though strangulation is present, because of obstruction at the hernial orifice. Left shoulder pain and hiccoughing, though observed infrequently, are important symptoms when present. Owing to displacement of the heart and lungs respiratory embarrassment, cyanosis, tachycardia and hypotension are commonly observed. Extravasation of bloody fluid contributes to the state of shock. Local signs over the chest include dullness or tympany, absent breath sounds and occasionally splashing and sucking sounds. Examination of the abdomen is negative unless bowel is also included in the hernia, in which case evidence of intestinal obstruction is usually found.

Roentgenographic findings should permit the correct diagnosis in the majority of cases. In a few cases, as in our case 4, a large pneumostomach may be present and can be confused with tension pneumothorax or with hemopneumothorax. However, collapsed lung is not seen against the mediastinum but is found compressed into the apex of the hemithorax. With less distention of the stomach the diaphragm may appear to be high, whereas the upper margin of opacity really represents the superior border of the stomach. Indeed, the herniated organ may be hidden behind the heart shadow. An upright chest x-ray film may reveal the presence of a gas bubble which is helpful in localizing the stomach. The heart is shifted toward the right, an important observation, since the fluid in the thorax is insufficient to cause this degree of displacement. After passage of a stiff gastric tube, implemented, if necessary, with lipiodol or barium instillation, the stomach can usually be localized above the diaphragm. However, because of obstruction at the hernial ring, it is not to be assumed that either the stomach tube or contrast medium will invariably find its way into the herniated portion of the stomach, and indeed the passage of a tube through the cardia may occasionally prove impossible in the presence of torsion or pressure upon the cardia by the distended stomach.

Pleural effusion resulting from primary lung or subdiaphragmatic pathology may occasionally require differentiation, but should not present the acute clinical picture seen in strangulated hernia.

Because of rapid deterioration from strangulated gastric hernia immediate surgery employing a thoracotomy approach is certainly indicated. If gangrene or perforation of the stomach is encountered, localized resection of the involved stomach with reestablishment of the gastric continuity is the procedure of choice. Compromising measures of lesser magnitude are unlikely to succeed. The empyema resulting from gastric perforation and the thoracogastric fistula produced by drainage of an empyema create enormous problems in the management of the patient. Subsequent surgery will have to be carried out on a greatly depleted patient in the presence of collapsed lung needing decortication.

SUMMARY

1. Seventeen cases of strangulated diaphragmatic hernia with gangrene and perforation of the stomach have been reviewed from the literature and two additional cases reported.
2. The clinical picture is described in detail.
3. Two cases of incarceration of the stomach with acute gastric dilatation are described to emphasize the ease with which a cursory examination may lead to the erroneous diagnosis of tension pneumothorax.
4. We have stressed the urgency of immediate surgery to avoid the complication of strangulation and possible perforation.

RESUMEN

1. Se han revisado 17 casos de hernia diafragmática estrangulada con gangrena y perforación del estómago según la literatura y se relatan dos casos más.
2. Se describe el cuadro clínico en detalle.
3. Dos casos de encarcelación del estómago con dilatación aguda gástrica se describen para recalcar la facilidad con que un examen corriente puede conducir al diagnóstico erróneo de neumotórax hipertensivo.
4. Hemos hecho notar la urgencia de la cirugía inmediata para evitar la complicación de la estrangulación.

RESUMÉ

1. 17 cas de hernie diaphragmatique étranglée avec gangrène et perforation de l'estomac signalés dans la littérature sont étudiés par les auteurs qui rapportent deux cas supplémentaires.

2. Le tableau clinique est exposé en détail.
3. Deux cas d'incarcération de l'estomac avec dilatation gastrique aiguë sont décrits. Ils permettent de mettre l'accent sur la facilité avec laquelle un examen superficiel peut amener au diagnostic erronné de pneumothorax sous tension.
4. Les auteurs insistent sur l'urgence d'un acte chirurgical immédiat pour éviter la complication possible d'étranglement et de perforation.

ZUSAMMENFASSUNG

1. Aus dem Schrifttum wurden 17 Fälle einer Zwerchfellhernie mit Strangulation, Gangrän und Perforation des Magens zusammengestellt und über 2 weitere eigene Fälle berichtet.
2. Das klinische Bild wird im einzelnen beschrieben.
3. Beschreibung von 2 Fällen mit Inkarceration des Magens und akuter gastrischer Dilatation zwecks Betonung der sehr naheliegenden Gefahr, dass eine kursorische Untersuchung zu der falschen Diagnose eines Spannungspneumothorax führen kann.
4. Wir haben die Dringlichkeit eines sofortigen Eingriffs besonders hervor gehoben zur Vermeidung der Komplikation einer Strangulation und möglichen Perforation.

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Results of Out-Patient Anti-Tuberculous Chemotherapy after Discharge from the Hospital*

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Introduction

The irregular discharge of pulmonary tuberculosis patients has always been an important public health problem. The question has been the topic of numerous papers in recent years. Attempts have been made in these studies to discuss the cause and prevention, and to analyze the "after-history" of once hospitalized patients in respect to the various factors involved. In view of the general employment of prolonged chemotherapy in post-hospitalized patients since about 1953, it was thought advisable to present a follow-up study of a group of patients after discharge from the hospital, and to attempt to provide an adequate basis for prognosis when prolonged out-patient chemotherapy is used.

The discharges during 1954 and 1955 were selected so that there could be at least two years or more of follow-up. It was considered unwise to go farther back because earlier chemotherapy regimes were less standardized. On the other hand, the 1956 and later discharges were not included because of insufficient follow-up. The regular discharges were also listed for the purpose of comparison.

Only combinations of isoniazid, PAS, and streptomycin were administered to out-patients. A few patients received the drugs for an indefinite term (over two years) because of their poor clinical condition or massive extent of their disease. The average length of out-patient chemotherapy was about 11.8 months.

Material and Observation

Four hundred fifty two patients discharged from Benjamin Franklin Hospital between January 1st, 1954 and December 31st, 1955 were selected from a total live discharge population of 561 of whom 227 were irregularly, and 225 regularly discharged. To avoid distorting the picture we are trying to present (the result of chemotherapy in active reinfection tuberculosis), certain categories of patients were eliminated from the list, such as extra-pulmonary tuberculosis, primary tuberculosis in children, pleural effusion, miliary tuberculosis, silico-tuberculosis, and non-tuberculous chest diseases. The numbers indicated in Table 1 represent the total number of patients rather than the total number of discharges. Some patients had more than one admission or discharge during the specified period. In March, 1958 all of the pertinent data were collected, representing from 27 to 50 months post-hospital follow-up.

Since relapse rate and mortality increase with extent of original disease, all of the patients were classified according to the admission diagnosis. To avoid confusion the revised discharge diagnoses were ignored during the study (Table 1).

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TABLE 1 — CLASSIFICATION OF EXTENT OF DISEASE, AND ADMISSION & DISCHARGE SPUTUM

	Irregular Discharge (227 patients)			Regular Discharge (225 patients)		
	Patients	Per cent with + sputum on admission	Per cent with + sputum on discharge	Patients	Per cent with + sputum on admission	Per cent with + sputum on discharge
FA	128	94 per cent	36.8 per cent	105	88.5 per cent	0 per cent
MA	65	66 per cent	18.5 per cent	77	60.0 per cent	0 per cent
MIN.	34	59 per cent	2.9 per cent	43	46.5 per cent	0 per cent

The far-advanced group consists of more than 50 per cent of the total number of patients studied. The average ages of regularly discharged patients were from 2.1 years to 6.9 years older than those irregularly discharged when separately considered according to extent of disease. This may indicate that chronological maturity may also bring about some emotional stability. As far as racial difference is concerned, the over-all census of the hospital population showed about 66 per cent white and 34 per cent non-white. The irregularly discharged group ranged from 69.5 per cent white patients in the far-advanced group to 88.3 per cent in the minimal group. Therefore, proportionally more white patients receive irregular discharges. The data regarding the length of hospitalization is interesting in that the irregularly discharged patients stayed in the hospital slightly over 60 per cent as long as the regularly discharged groups. This was 298 days versus 475 days in far-advanced cases, 169 versus 280 days in moderately-advanced disease, and 136 versus 207 days in minimal cases.

Table 1 shows the sputum status on admission and on discharge. Only those with negative sputum received regular discharges. The fact that a high percentage of irregularly discharged patients with minimal and moderately-advanced disease had negative sputum at the time of discharge is significant. It is probably due in part to relatively long hospitalization, which amounted to 60 per cent of the duration of hospitalization for regular discharges.

Table 2 shows that about 3.8 per cent of the patients could not be located following discharge. Slightly over 50 per cent are currently under the supervision of the county tuberculosis clinic, and another 13.5 per cent were followed by private physicians in this city and county. Frequent communication between the Tuberculosis Controller's Office and the local private physicians result in very accurate up-to-date information about private patients. Those who moved out of the county constitute 17.2 per cent. Information about these patients was frequently obtained through various public health authorities.

The total mortality in 452 was 9.1 per cent, but when the statistics were presented according to their original disease there was definitely a high mortality rate among the far-advanced group. Of a total of 41 deaths, 22 were in the far-advanced irregularly discharged group (Table 2). The adjusted mortality (non-tuberculous deaths omitted) presented a quite different picture. Only the far-advanced disease patients had deaths; 14.1 per cent in the irregular group and 6.6 per cent in the regu-

TABLE 2 — CURRENT STATUS OF PATIENTS CLASSIFIED ACCORDING TO ORIGINAL EXTENT OF DISEASE

Status/ Classification	FA (233)				MA (142)				MIN. (77)					
	Irregular (128)		Regular (105)		Irregular (65)		Regular (77)		Irregular (34)		Regular (43)		TOTAL	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
Dead	22	17.2	11	10.4	2	3.2	2	2.6	1	2.9	3	7.0	41	9.1
Hospitalized	20	15.6	2	1.9	1	1.8	1	1.3	1	2.9	1	2.3	26	5.7
Followed in Clinic	45	35.2	62	59.0	33	50.2	48	62.5	18	53.0	23	53.5	229	50.7
Under Private Care	12	9.4	10	9.6	11	17.0	16	20.6	5	14.7	7	16.3	61	13.5
Out-of-County	26	20.3	16	15.3	14	21.6	8	10.4	6	17.7	8	18.6	78	17.2
Not Found	3	2.3	4	3.8	4	6.2	2	2.6	3	8.8	1	2.3	17	3.8
TOTAL	128	100.0%	105	100.0%	65	100.0%	77	100.0%	34	100.0%	43	100.0%	452	100.0%

lar group. There was no death in either the moderately-advanced or minimal cases, regardless of whether they were regularly or irregularly discharged.

The average length of hospitalization of irregularly discharged patients who died of tuberculosis was 628 days, and the average length of hospitalization of those regularly discharged who died of tuberculosis was 820 days, so the conclusion could be drawn that most far-advanced irregularly discharged patients were rather hopeless and desperate cases, and even if they had remained in the hospital they probably would have succumbed to the disease within two to three years. Actually, many of them were readmitted, and died in the hospital.

The readmission rates were selected as a yard-stick to measure the complicated problem of relapse rate. In order to avoid hopeless complexity, one has to resort to broad generalization in grouping the cases, and the writers recognize that it is difficult to avoid over-simplification. However, some significant and pertinent facts were obtained through this crude study. A patient is readmitted only under the following few conditions: Positive sputum, roentgenographic spread, worsening clinical condition, or such complications as hemoptysis, spontaneous pneumothorax, etc. The overall readmission rate between various groups is strikingly different between the regular and irregular discharge groups. The readmission rate of regularly discharged patients shows approximately the same percentage regardless of the extent of their disease; it varies from 7 per cent in minimal cases to 10.8 per cent in the far-advanced group.

The irregular discharge groups demonstrated a different picture. The readmission rate was 98.5 per cent in the far-advanced group, 50 per cent in the moderately-advanced group, and even in the minimal group the rate was a surprisingly high 41.2 per cent (Table 3).

The data on out-patient chemotherapy were compiled according to three possible outcomes: (1) Those who completed the prescribed length of chemotherapy (2) Those continuing on therapy (3) Those who had interrupted the treatment against medical advice. It is shown in Table 3 that whenever patients did not follow through the whole length of treatment on out-patient basis, the readmission rates are higher than those who had completed the prescribed course.

Because of possible variation in treatment regimens, the chemotherapy data was omitted on patients who were either under private care or out-of-county.

Table 4 summarizes the current clinical activity of all traceable surviving patients. Those who died or were out of the county were omitted. Activity is classified according to the National Tuberculosis Association standards. All so-called "open-negative" cases were classified as active, so the percentage figure is heavily weighted in favor of active disease. Out-of-county patients were not included in the table because of possible difference of opinion in classifying cases in various localities.

Eight of the irregularly discharged patients had open cavity at the time of discharge and had negative sputum for at least one year prior to discharge. Four of the eight have shown no x-ray film change since discharge, and the other four have shown some improvement, one with

TABLE 3 — CORRELATION OF OUT-PATIENT CHEMOTHERAPY WITH READMISSIONS

		FA (233)				MA (142)				MIN. (77)			
		Irregular (128)		Regular (105)		Irregular (65)		Regular (77)		Irregular (34)		Regular (43)	
		No. of Patients	No. of Readm.	No. of Patients	No. of Readm.	No. of Patients	No. of Readm.	No. of Patients	No. of Readm.	No. of Patients	No. of Readm.	No. of Patients	No. of Readm.
Dead	RX Completed	3	2	2	0	0	0	2	0	1	0	2	0
	On RX at death	5	7	3	2	0	0	0	0	0	0	0	0
	RX Interrupted	14	25	6	1	2	4	0	0	0	0	1	0
Hospitalized	RX Completed	1	3	1	1	0	0	0	0	0	0	0	0
	RX Continuing	4	6	0	0	0	0	1	1	0	0	0	0
	RX Interrupted	16	35	1	1	1	2	0	0	1	3	1	1
Followed	RX Completed	13	3	44	0	13	2	36	1	9	2	16	1
In Clinic	Now on RX	8	5	2	0	4	1	1	1	1	0	0	0
	RX Interrupted	22	16	16	0	16	13	11	3	8	2	7	0
Under Private Care	RX ?	12	2	10	2	11	1	16	0	5	0	7	0
Out-of-County	RX ?	28	20	16	1	14	8	8	2	6	7	8	1
Not Found	RX ?	3	2	14	3	4	1	2	0	3	0	1	0
Total Number		128	126	105	11	65	33	77	8	34	14	43	3
Readm./Patient Per cent		98.5 per cent		10.8 per cent		50 per cent		10.6 per cent		41.2 per cent		7 per cent	

TABLE 4 — TRACEABLE SURVIVORS CURRENTLY WITH ACTIVE TUBERCULOSIS

	Regular (170)		Irregular (146)	
	Number of Patients	Per cent	Number of Patients	Per cent
FA	12	7.1	33	22.5
MA	2	1.2	5	3.4
MIN.	1	0.6	1	0.7
Total patients with Active Tuberculosis	15	8.9	39	26.6
Total patients with Inactive Tuberculosis	155	91.1	107	73.4

cavity closure. Among regularly discharged traceable survivors 91.1 per cent have inactive disease, as compared with 73.4 per cent in the irregularly discharged group.

Comment

Certain facts obtained from the tables deserve emphasis. Only 26.6 per cent of traceable surviving irregularly discharged patients still had active tuberculosis after two to three years of follow-up; about 85 per cent of these had far-advanced tuberculosis. In the regularly discharged group, 75 per cent of the active cases were far-advanced. The fact that patients in only the far-advanced group died due to tuberculosis points out further that, as would be expected, far-advanced disease has a definitely poorer prognosis from moderately-advanced or minimal disease. One explanation of this fact is obvious — there is no upper limit of extent of tuberculosis in the far-advanced cases.

Observations such as the present study are not a measure of long-term effectiveness of any particular drug regimen. Instead, they are more a measure of judgment exercised by the physicians who supervise, change and terminate the various drugs according to the circumstances.

No attempt was made here to discuss the cause or the prevention of irregular discharges. This subject has been discussed rather extensively by others; however, a brief statement might be in order. Our irregularly discharged patients averaged about 44 per cent of live discharges from January, 1951 through September, 1957, and it dropped to 25 per cent since October 1, 1957 when an Isolation Ward in the City Workhouse became available.

Collapse therapy was continued in only a few patients. The total number was so small that no separate figures were tabulated.

The limitations of the present study were clearly recognized from the beginning. The records of many of the irregularly discharged patients indicated a long-standing lack of cooperation in both medical supervision and observation of precautions against the spread of their disease. Clinic appointments have been kept irregularly or not at all. With the institution of out-patient chemotherapy in these patients, we had hoped that the drug would induce them to attend the clinic more regularly.

It is apparent from the study of readmission rates that even the irregularly discharged patients who faithfully take anti-tuberculous drugs stand a fair chance of getting well.

We are not in sympathy with the view held by many that the patient who leaves the hospital against advice should be denied out-patient chemotherapy either as a punitive measure, or as a deterrent to others who may be tempted to leave the hospital. We believe that the public health will best be served by intensive chemotherapy of all active tuberculosis.

It is our intention to pursue this study further by collecting data on these patients for several more years in order to get a long-term follow-up.

SUMMARY

A group of 452 discharged tuberculosis patients was presented with results of post-hospital chemotherapy. It was found that relapse and mortality were higher in those patients who had interrupted their treatment, and that the prognosis of even irregularly discharged patients was good if they continued chemotherapy faithfully.

RESUMEN

Se presentó un grupo de 452 enfermos de tuberculosis con los resultados de quimioterapia después de salidos del hospital.

Se encontró que la recaída y la mortalidad fueron más elevados entre los que abandonaron su tratamiento y que el pronóstico, aún de los que tuvieron alta hospitalaria irregular, fué mejor si continuaban la quimioterapia con fe.

RESUMÉ

L'auteur présente un groupe de 452 malades tuberculeux sortis de l'hôpital, avec les résultats de la chimiothérapie post-hospitalière. Rechute et mortalité furent plus élevées chez les malades qui avaient interrompu leut traitement et le pronostic des malades même sortis irrégulièrement de l'hôpital est bon s'ils ont consciencieusement continué la chimiothérapie.

ZUSAMMENFASSUNG

Bericht über eine Gruppe von 452 entlassenen tuberkulösen Patienten mit Ergebnissen der sich an die stationäre Behandlung anschliessenden Chemotherapie. Es wurde festgestellt, dass Rückfälle und Sterblichkeit höher waren unter den Kranken, die ihre behandlung unterbrochen hatten, und dass die Prognose selbst bei ohne ärztliche Zustimmung entlassenen Patienten gut war, sofern sie ihre Chemotherapie ordnungsgemäss weiterführten.

Chest Wall Tumors

A review of clinical experiences with 30 cases.*

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Tumors of the chest wall, although not uncommonly encountered, have received relatively little attention in the literature. In view of this, we are prompted to present a review of our clinical experiences with 30 such tumors particularly to emphasize their insidious nature and the consequent necessity for early and adequate surgical extirpation. The clinical features of benign and malignant chest wall tumors will be reviewed and the principles of their surgical management discussed. The sequence of inadequate primary excision of an ostensibly benign tumor followed by repeated local recurrences and ultimately by widespread metastases is tragically documented in several of our cases. Also, two cases are included in which a metastatic chest wall tumor provided the sole clue to the location and nature of a silent primary neoplasm.

In 1933, Hedblom[1] reviewed the world literature and collected 291 cases of tumors of the osseous structures of the chest wall to which he added 22 cases of his own. Thereafter, Sommer and Major,[2] in 1942, summarized an additional 66 cases recorded in the world literature from 1933 to 1940 and added 15 cases from the thoracic surgical service of the University of Michigan. No further review of the subject appeared until Blades and Paul[3] summarized their experiences with 53 chest wall tumors in 1950. From 1950 to the present, there have been isolated case reports of chest wall tumors, generally dealing with the complexities and technics of repair of large chest wall defects following surgical excision. To our knowledge, however, there have been no further reviews of clinical experiences with chest wall tumors as a group.

In view of the inconsistency of the clinical behavior of certain of these lesions with their pathological appearance, we feel that it is appropriate to employ a clinical classification, as suggested by Blades and Paul, of (1) benign; (2) malignant; and (3) metastatic chest wall tumors. All of the tumors included in this report were encountered in a practice restricted to thoracic surgery so that the many varieties of neoplasms of the skin and subcutaneous tissues which are not clinically fixed to the deeper structures of the chest wall are automatically excluded. In addition, we have excluded all metastatic tumors of the chest wall except those which were solitary and originated from a silent primary neoplasm. Accordingly, these metastatic lesions clinically appeared to be primary chest wall neoplasms.

Benign Tumors — 17 cases

Upon referring to Table 1 it is noted that the largest category of benign chest wall tumors is comprised of the neurogenic group. In our experience, these tumors were frequently asymptomatic and discovered on

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routine survey chest x-ray films. The symptomatic neurogenic tumors were productive of pain, either constant and dull, as in the neurofibromas and ganglioneuromas, or intermittent, sharp and lancinating, as in the one case of intercostal neuroma which we encountered. In contradistinction to many other types of chest wall neoplasms which presented as palpable tumefactions, none of the neurogenic tumors were palpable on clinical examination and all of them exhibited varying degrees of intrapleural protrusion upon x-ray film examination. Characteristically, they produced a smooth discrete radiodensity which was convex centrally and based upon the chest wall peripherally (Figure 1). The neurofibromas and ganglioneuromas were generally located posteriorly and, at operation, were related to the intercostal nerves or sympathetic chain. Occasionally, it is difficult to differentiate these tumors from a peripheral pulmonary lesion without induction of a diagnostic pneumothorax.

Chondroma was the second commonest benign tumor encountered in our series (Table 1). These lesions presented clinically as gradually enlarging, palpable tumefactions associated, in one case, with mild local discomfort. They were all located anteriorly in the costal cartilages and could not be visualized radiologically. One of these cases was classified clinically as a post-traumatic chondroma in that there were two large chondromatous masses, one in each costal arch, which the patient ascribed to a steering-wheel type of chest injury four months previously. Pathologically, there was evidence of some recent inflammatory reaction in association with the chondromas.

Although each of these four patients remain well to date, it is with considerable trepidation that we report these lesions as "benign chondromas." As noted by Mallory,[4] although chondromas of the rib cage may appear benign histologically, they frequently exhibit a predisposi-

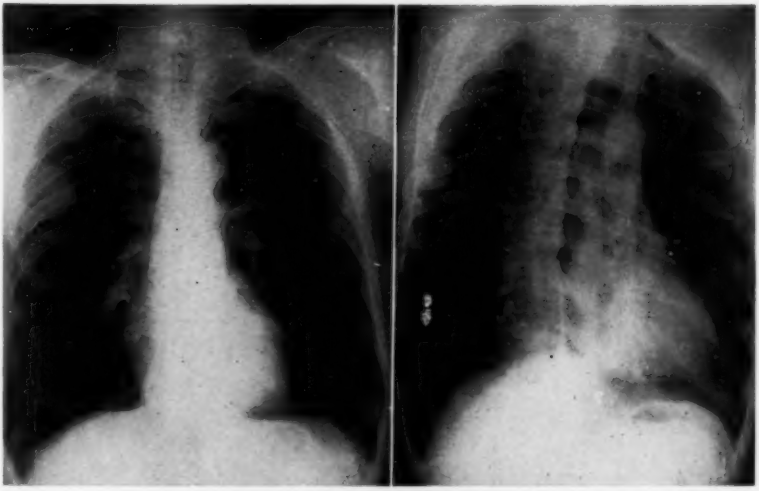

FIGURE 1: Neurofibroma exhibiting the characteristic features of neurogenic tumors: homogeneous, discrete radiodensity convex centrally and based upon the chest wall peripherally.

tion to local implantation with the ultimate development of frank malignancy and widespread metastases. Three of the five cases of chondrosarcoma in our series followed this pattern.

As in the cases of fibrous dysplasia reported by Blades and Paul, each of our three cases of fibrous dysplasia of rib gave a clear cut history of antecedent trauma to the area of involvement. In one of these cases, the lesion was discovered on a survey film whereas the other two patients reported for x-ray film examination because of the onset of localized chest discomfort. In each case, x-ray films revealed a localized osteolytic process within a rib (Figure 2). At operation, a well-circumscribed fusiform tumor mass involving the rib was uniformly found. Resection of these lesions resulted in permanent cure.

Only lipomas arising beneath the fascia propria of the chest wall musculature and thereby fixed to the deep structures of the chest wall were included in this series. For this reason, only two lipomas are reported; one arose deep to the left scapula and presented in the left posterior cervical triangle, and the second arose from the seventh left intercostal space anterolaterally and presented as a semi-fixed local tumor mass. In each case the development of a palpable tumor mass was the presenting complaint and in one there was also some associated local discomfort. In each case, excision necessitated a meticulous dissection of a lobulated tumor mass arising from the deep structures of the chest wall. These lesions, in contradistinction to the many superficial lipomas, should be excised only with the patient under general anesthesia in a major operating room where one is equipped to proceed with thoracotomy.

The remaining benign tumor of the chest wall which we encountered involved the sternoclavicular joint. A 57 year old white woman, had noted progressive swelling and tenderness of the right upper anterior chest region for a period of one year. The lesion clinically appeared to be a firm, non-tender circumscribed tumor mass involving the sterno-

FIGURE 2: Fibrous dysplasia of rib appearing as central osteolytic process surrounded by a ring of increased radiodensity.

clavicular joint. She had no other joint symptom. X-ray films were negative. At surgical exploration, a discrete tumor mass limited to the joint capsule was encountered and it was elected to proceed with a resection of the sternoclavicular joint. Postoperatively, she has been entirely relieved of her symptoms and has no deformity resultant from the excision. Pathologically, the tumor mass was reported to represent chronic papillary synovitis of the sternoclavicular joint.

Malignant Chest Wall Tumors — 13 cases

In this series of chest wall tumors, 13 of the 30 cases (43 per cent) were malignant. Two of the 13 malignant tumors were metastatic while the remaining 11 were primary. This compares with an incidence of malignancy of 47 per cent reported by Blades and Paul but, as they have pointed out, is an inaccurate reflection of the total incidence of malignancy among chest wall tumors since the preponderantly benign lesions of the skin and subcutaneous tissues not clinically fixed to the chest wall have been excluded. Nevertheless, we believe that the figure, 43 per cent, serves to reflect accurately on the high incidence of malignancy among the deep-seated chest wall tumors and should dispel any complacency in dealing with these neoplasms.

The pathologically benign-appearing chondroma is, perhaps, the most insidious of all chest wall tumors.[4] It must be resected adequately at the outset because of its propensity to implantation and local recurrence. Three of the five cases of chondrosarcoma in our series appeared initially as small, painless, tumors which were subjected to multiple biopsy procedures or inadequate local excisions over extended periods of time before their intrinsic malignant nature was recognized. In one case, the tumor mass was stable and asymptomatic for at least 10 years, when

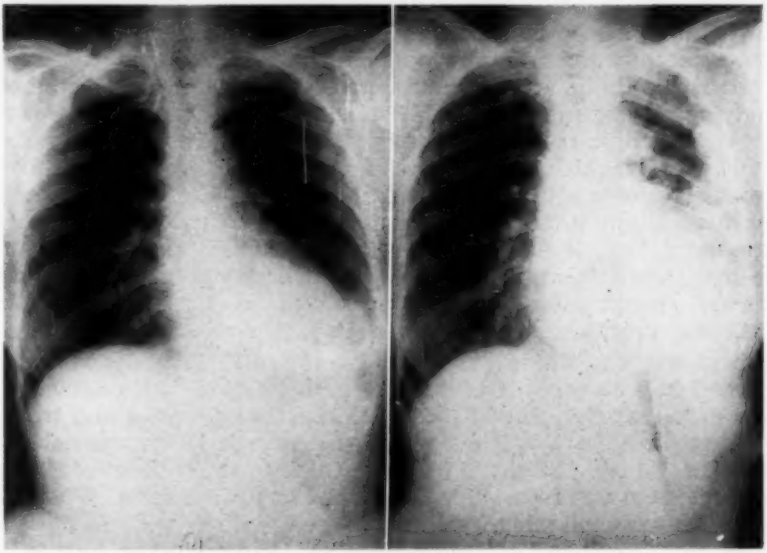

FIGURE 3A and B: A case of chondrosarcoma of rib illustrating the development of extensive pleural implantation metastases over a period of six years.

a gradual increase in size was noted. In retrospect, the primary surgical excision in this case and in two other cases, all done elsewhere, was inadequate but was tempered by the deceptive pathological diagnosis of benign chondroma. Recurrences occurred in all three cases despite the subsequent employment of extensive surgical resections. Two of the patients died as a result of both locally recurrent and metastatic chondrosarcoma and the third, although still alive six years after the primary operation, is in poor condition due to extensive implantation metastases both locally and throughout the entire ipsilateral pleural space (Figure 3A and B). Only in two of our five cases was an adequate primary en bloc resection performed. One of them, a 71 year old man, died on the third postoperative day of gastric dilatation and aspiration of vomitus. The other is living and well one year following surgery.

In contrast to the benign chondromas, which frequently appear during adolescence and early adulthood, the chondrosarcomas generally appear during middle or late adulthood. The sex incidence is essentially evenly divided. All of the chondrosarcomas in our series were located in the anterior chest wall.

The remaining six cases of primary malignant tumors of the chest wall in our series are representative of six different types of tumors, including five varieties of sarcoma and a localized plasma cell myeloma. (Table 2) We encountered one case of osteogenic sarcoma of rib occurring in a 61 year old white man. These tumors are less frequently found in the ribs and sternum than are the chondrosarcomas. Only 1 to 3 per cent of osteogenic sarcomas occur in the osseous structures of the chest wall. The primary symptomatology in our patient was that of pleuritic chest pain and associated cough dating back some 10 months. X-ray films revealed a mass arising in the right fifth rib and protruding intrapleurally. At operation, the tumor mass, although bulging intrapleurally, did not invade the parietal pleura. The involved rib and adjacent intercostal muscles and pleura were resected en bloc. Upon exploration of the mediastinum at this time we were chagrined to find a firm node overlying the superior vena cava. This node was excised and was reported to contain metastatic osteogenic sarcoma. The patient was readmitted two months later because of acute femoral arterial thrombosis ultimately necessitating amputation of the right leg. He expired shortly thereafter and post mortem examination was conducted which revealed extensive metastatic sarcoma in the left (contralateral) pulmonary hilum, the liver, adrenals, and abdominal peri-aortic lymph nodes. Although osteogenic sarcomas classically engender hematogenous metastases, this particular tumor had spread both hematogenously and lymphogenously.

There was one Ewing's sarcoma in our series. This lesion, which occurred in a 30 year old white woman, manifested itself originally as a tumor mass arising in the left clavicle. It was biopsied and treated intensively with x-ray. Three years later a cystic lesion was noted in the left third rib. Excisional biopsy of the involved segment of rib was performed and was reported to show only fibrous dysplasia. When last seen, nine years following treatment, she was entirely well. As reported previously,[3] biopsy and radiotherapy rather than radical excision is the treatment of choice for Ewing's sarcoma.

Three other sarcomatous lesions were encountered: a malignant mesenchymoma, a recurrent neurogenic sarcoma and a hemangioendothelial sarcoma. The malignant mesenchymoma presented as an inflammatory tumor mass in the chest of a 56 year old man and was erroneously thought to represent an abscess or hematoma requiring incision and drainage. This procedure had already been carried out when we first saw him (Figure 4). An en bloc resection of the chest wall to circumscribe the entire tumor mass was then effected, necessitating resection of the 9th, 10th, and 11th ribs together with a portion of the diaphragm and the upper abdominal musculature. His convalescence was marred by the development of mechanical small bowel obstruction which, at laparotomy, was found to be due to a sarcomatous peritoneal implant. Resection and anastomosis was carried out. He expired a few months later of metastatic sarcoma.

The recurrent neurogenic sarcoma appeared about two years following local excision elsewhere of a small painless nodule in the anterior chest wall of a 52 year old man. A radical resection of the chest wall to include the entire area of recurrence was carried out without difficulty. He is entirely well four years postoperatively.

The hemangioendothelial sarcoma presented as a painful tumor mass in a 57 year old woman. X-ray film study revealed an osteolytic process in the right 10th rib associated with a surrounding tumor mass. En bloc excision was carried out but an extensive local recurrence developed which was refractory to irradiation and she expired a few months later.

The plasma cell myeloma of rib was discovered on a routine survey chest film. It appeared as a triangular area of density in the right anterior thorax. (Figure 5.) This 47 year old white man was subjected to a wide resection of the tumor mass including a segment of adjacent uninvolved rib on either side of the tumor. Seven years postoperatively he continued to be entirely well.

FIGURE 4: Malignant mesenchymoma which presented as an inflammatory mass and had already been subjected to an ill-advised "incision and drainage."

Metastatic Tumors — Two cases

The first of these patients, a 55 year old man, developed a painless nodule in the right anterior chest wall. Chest x-ray films revealed an osteolytic process in the right third rib with apparent expansion of the cortex in this area. Both lung fields were clear. An excisional biopsy was performed and frozen section revealed squamous cell carcinoma of pulmonary origin. He was lost to follow-up for a period of almost eight months, at which time repeat chest x-ray films revealed a large hilar mass on the left (contralateral) side suggestive of bronchogenic carcinoma. This lesion was deemed categorically inoperable and he died shortly thereafter. In our entire experience with bronchogenic carcinoma, this was the only example of a metastatic chest wall lesion appearing before the primary pulmonary lesion could be detected. Without question, the chest wall lesion in this case represented an early hematogenous metastasis, excision of which promptly established both the diagnosis and prognosis, and obviated exploratory thoracotomy.

The second patient was a 55 year old white man who had noted the development of progressively severe left chest pain over a period of two months. Clinical examination revealed a non-tender fusiform mass within the posterolateral portion of the left fifth rib. Chest films demonstrated an osteolytic lesion. At operation, a fusiform tumor mass was noted to replace the posterolateral portion of the left fifth rib. Biopsy and frozen section examination indicated that the tumor was a metastatic carcinoma. Accordingly, a simple segmental resection of the tumor-bearing portion of the rib was performed. Microscopic study of the permanent sections established a diagnosis of metastatic Hurthle cell carcinoma. Subsequently, a total thyroidectomy was done and a microscopic Hurthle cell "adenoma" was found in one section of the gland. He was then given a therapeutic dose of radioactive iodine followed by total body screening but no concentrated area of uptake was observed. He is cur-

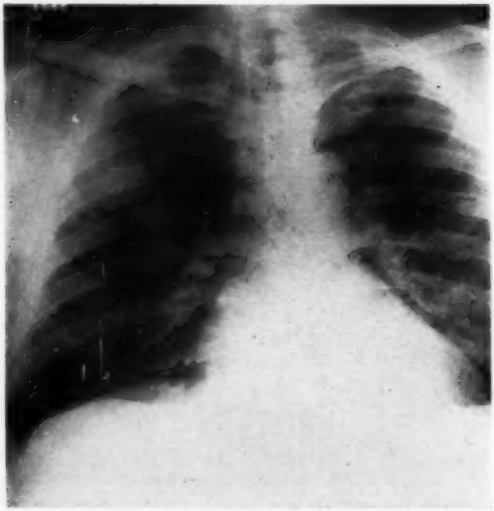

FIGURE 5: Plasma cell myeloma involving right third rib anteriorly.

FIGURE 6A: Chondrosarcoma of the sternum which had been biopsed several times over a period of years with a diagnosis of "benign chondroma" being returned on each occasion.

FIGURE 6B: Postoperative status following total excision of body of sternum, costal cartilages and underlying pericardium with repair by shifting flaps and split-thickness skin grafting.

TABLE 1 — BENIGN CHEST WALL TUMORS — 17 cases (57 per cent)

Neurogenic Tumors	7	Fibrous Dysplasia	3
Chondroma	4	Lipoma	2
Chronic Papillary Synovitis sternoclavicular joint			1

rently entirely well eight months following surgery. In this case, biopsy and frozen section study indicated that the tumor was a metastatic carcinoma. A radical resection of the chest wall was thereby obviated. Whether or not this patient has been permanently cured of his carcinoma, it is certain that early excision of the chest wall metastasis, in combination with the other therapeutic measures, has afforded him excellent palliation and will prolong the period of his useful existence.

Results

The results of our experience with malignant chest wall tumors can be summarized by stating that of the 11 patients with primary malignancies, six have died, five of recurrent or metastatic disease, and one of a postoperative complication (Table 3). Of the five survivors, one has extensive recurrent malignancy. Accordingly, there are four (36 per cent) in the primary malignancy group who are living and well following surgery. These include a chondrosarcoma case which has only been followed for slightly more than one year after surgery; the Ewing's sarcoma, nine years following surgery and irradiation; the neurogenic sarcoma, four years following radical re-operation; and the plasma cell myeloma, seven years following radical excision.

Surgical Considerations

All primary chest wall tumors should be subjected to early and adequate excision. This almost invariably should involve a thoracotomy approach, entering the pleural space two or more interspaces above or below the tumor in order to evaluate the nature and extent of pleural involvement. If one is reasonably secure in the belief that the tumor is benign, a thorough local excision is accomplished and the specimen is sent for frozen section microscopic study. A radical re-excision of the

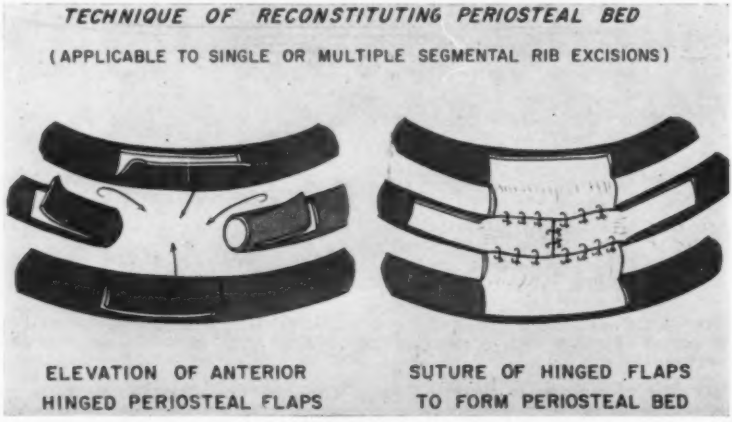
TECHNIQUE OF RECONSTITUTING PERIOSTEAL BED
(APPLICABLE TO SINGLE OR MULTIPLE SEGMENTAL RIB EXCISIONS)
ELEVATION OF ANTERIOR HINGED PERIOSTEAL FLAPS
SUTURE OF HINGED FLAPS TO FORM PERIOSTEAL BED

FIGURE 7

TABLE 2 — MALIGNANT CHEST WALL TUMORS—13 cases (43 per cent)

1. Primary Malignancies	
Chondrosarcoma	5
Osteogenic Sarcoma	1
Ewing's Sarcoma	1
Malignant Mesenchymoma	1
Neurogenic Sarcoma	1
Hemangioendothelial Sarcoma	1
Plasma Cell Myeloma	1
	11
2. Solitary Metastatic Malignancies (Silent Primary)	
From Lung (Squamous Cell Carcinoma)	1
From Thyroid (Hurthle Cell Carcinoma)	1
	2

entire wound can be carried out if warranted by the frozen section report. In the case of metastatic tumors, the primary local excision should suffice. If the tumor clinically appears to be malignant, particularly if it represents a recurrence of a previously excised tumor, a primary radical resection should be performed, resecting at least one uninvolved rib and intercostal bundle above and below the tumor mass, together with a wide portion of any adjacent involved tissue such as upper abdominal or chest wall musculature, diaphragm, lung, pericardium, etc.

The chief problem arises in dealing with the potentially malignant neurogenic tumors and especially the chondromas, which may appear benign clinically and upon microscopic study. Presently, it is our policy to content ourselves primarily with an adequate total excisional biopsy and to follow these patients closely for several years postoperatively. As previously noted, the malignant chondromas particularly tend to implant and recur locally repeatedly before giving rise to distant metastases. At the first indication of local recurrence, a radical resection should be carried out.

Numerous technics have been devised to repair the chest wall defects which attend excision of these tumors. Recently, attention was centered upon the employment of prostheses of various types. Our own experience coincides with that of Blades and Paul in that we have been able to effect repair of even the most extensive defects by shifting muscles flaps, employing releasing incisions in the skin and utilizing skin grafting procedures. One case of chondrosarcoma involving the sternum had been biopsied several times over a period of years and on each occasion a diagnosis of chondroma was returned. At the time we saw the patient, a

TABLE 3 — RESULTS OF TREATMENT (Primary Malignancies)

	Dead	Living with Recurrence	Living and Well	
Chondrosarcoma (5)	3	1	1	(1 yr.)
Osteogenic Sarcoma (1)	1			
Ewing's Sarcoma (1)			1	(8 yrs.)
Malignant Mesenchymoma (1)	1			
Neurogenic Sarcoma (1)			1	(4 yrs.)
Hemangioendothelial Sarcoma (1)	1			
Plasma Cell Myeloma (1)			1	(7 yrs.)
Total Cases (11)	6	1	4	(36%)

large ulcerating tumor mass bulged from the body of the sternum (Figure 6A.) and necessitated an extensive resection of the entire sternal body including the adjacent costal cartilages and underlying pericardium. Even this huge post-resectional defect could be satisfactorily closed by the use of plastic surgical technics. (Figure 6B.) Figure 7 demonstrates diagrammatically a technic which we employ to reconstitute the periosteal bed following segmental resection of one or more ribs. This technic has been applied by one of us (D. C. D.) for more than 10 years and has effectively eliminated the persistence of soft areas postoperatively in the chest wall.

SUMMARY

Our clinical experience with a group of 30 chest wall tumors, of which 13 (43 per cent) were malignant, has been presented. The neurogenic tumors were found to be the commonest of the benign neoplasms whereas the chondrosarcomas were the most frequently encountered of the malignant neoplasms. Two metastatic tumors were documented, each masquerading as a primary chest wall tumor.

The surgical approach to tumors of the chest wall was discussed, emphasizing the importance of early and adequate primary excision by thoracotomy approach, and radical re-excision when indicated by study of the excised specimen. It is our opinion that early radical excision will result in a much higher salvage rate, especially for the chondrosarcomas. One can assume that almost half of the deep-seated chest wall tumors will prove to be malignant. Repair of the chest wall defects resulting from radical excisional procedures was found to be most easily effected by means of plastic technics. The use of prosthetic materials was unnecessary in our experience.

RESUMEN

Nuestra experiencia clínica con un grupo de 30 tumores de la pared del tórax de las que 13 (43 por ciento) fueron malignos, es el objeto de este trabajo.

Los tumores neurógenos son los más comunes de las neoplasias benignas en tanto que los condrosarcomas fueron los más frecuente de los malignos.

Dos tumores metastásicos fueron comprobados, en cada caso aparecieron como si fueran primitivos.

Se diserta sobre el tratamiento quirúrgico de estos tumores recalcando la importancia de la extirpación temprana y adecuada por la toracotomía así como por la reexcisión cuando estaba indicada por el estudio del especimen resecado. Somos de opinión que la excisión radical produce mayor proporción de curaciones, especialmente para los condrosarcomas.

Puede uno suponer que como la mitad de los tumores de la pared del tórax profundamente situados son malignos. La reparación de la pared defectuosa por la resección de estos tumores fué más fácil de efectuarse por las técnicas plásticas. En nuestra experiencia no se necesitó el uso de materiales protésicos.

RESUMÉ

L'auteur rapporte l'expérience clinique qu'il a pu tirer de l'étude de 30 tumeurs de la paroi thoracique, parmi lesquelles 13 (43%) étaient malignes. Les tumeurs d'origine nerveuse se trouvèrent être les plus communes des néoplasies bénignes, tandis que les chondrosarcomes furent les plus fréquents des néoplasies malignes. Des recherches furent faites sur deux tumeurs métastatiques, qui se présentaient chacune sous les traits d'une tumeur primitive de la paroi thoracique.

L'indication chirurgicale pour les tumeurs de la paroi thoracique est discutée, en mettant l'accent sur l'importance d'une première exérèse convenable par thoracotomie d'abord, puis par intervention radicale si elle est indiquée après étude de l'échantillon prélevé. L'opinion de l'auteur est qu'une exérèse radicale précoce doit donner un pourcentage plus élevé de sauvetages surtout pour les chondrosarcomes. On peut admettre que presque la moitié des tumeurs de la paroi thoracique profondément situées feront la preuve de leur malignité. L'auteur pense que la réparation des altérations thoraciques après exérèse radicale est plus facilement effectués grâce aux techniques plastiques. L'utilisation de matériaux de prothèse ne fut pas nécessaire dans son expérience.

ZUSAMMENFASSUNG

Darstellung unserer klinischen Erfahrungen an einer Gruppe von 30 Brustwandtumoren, von denen 13 (43%) bösartig waren. Es zeigte sich, daß die neurogenen Tumoren unter den gutartigen am häufigsten vorkommen, während die Chondrosarkome die häufigsten bösartigen Formen darstellten. Wiedergabe von 2 Fällen mit metastatischen Tumoren, von denen jeder sich als primäre Brustwandgeschwulst maskiert hatte.

Besprechung des chirurgischen Vorgehens bei solchen Brustwandtumoren unter Betonung der Wichtigkeit frühzeitiger und ausgiebiger primärer Excision auf dem Wege einer Thorakotomie. Radikale Re-Excision ist erforderlich, sofern die histologische Untersuchung des Operationspräparates dies angezeigt erscheinen läßt. Nach unserer Meinung ergibt die frühzeitige radikale Excision eine weit bessere Heilungsziffer besonders bei Chondrosarkomen. Man kann annehmen, daß fast die Hälfte der tiefsitzenden Brustwandtumoren sich als bösartig erweisen. Behebung der Brustwanddefekte, die sich aus der Radikaloperation ergeben, erfolgt am Besten unter Zuhilfenahme plastischer Methoden. Der Gebrauch von Prothesen ist nach unserer Erfahrung nicht notwendig.

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Right Duct Lymph Flow in Dogs Measured by a New Method

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Warren and Drinker[1] had demonstrated that in the dog, lymph from all parts of the lung except the upper section of the left lung generally flowed to the right lymphatic duct. The right duct is of minute size and frequently presents with multiple channels.[2] Consequently, cannulation is extremely difficult; and when cannulation of one of the minute channels is successful, only representative flow is obtained. These technical factors have limited study of the pulmonary lymphatic drainage.[3] It is the purpose of this paper to introduce a new method for the collection of right duct lymph and present the data obtained by this method of collection in normal dogs.

Methods

Fifteen dogs were anesthetized with nembutal (29 mg./kg.) and given 10 to 12 cc. of T-1824 intratracheally. Respirations were maintained by

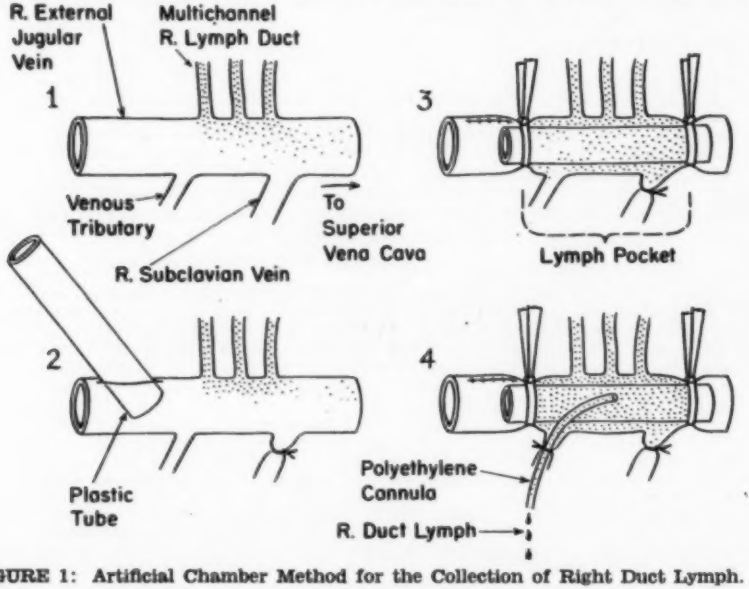

FIGURE 1: Artificial Chamber Method for the Collection of Right Duct Lymph.

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intermittent positive pressure. Right duct lymph was collected by the method illustrated in Figure 1.

This technique consists of creating an artificial chamber within the external jugular veins, in the vicinity of the entrance of the right lymphatic channels, through which is conducted the uncontaminated jugular venous blood. Fig. 1-1 shows a segment of the external jugular vein into which the multichannel right lymphatic duct enters. In Fig. 1-2 a plastic tube is inserted into the vein. The tube is pushed to approximate the entrance of the lymphatic channels and is secured, thus establishing a route for allowing continuity of the venous return and at the same time isolating a pocket into which the lymphatic channels enter. This permits the blood to return to the heart without mixing with the lymph flow. In Fig. 1-4 a venous tributary to the chamber is cannulated with a small polyethylene tube and the residual blood is aspirated. The tube then serves as an outflow channel for right duct lymph.* Flows were collected at 15-minute intervals.

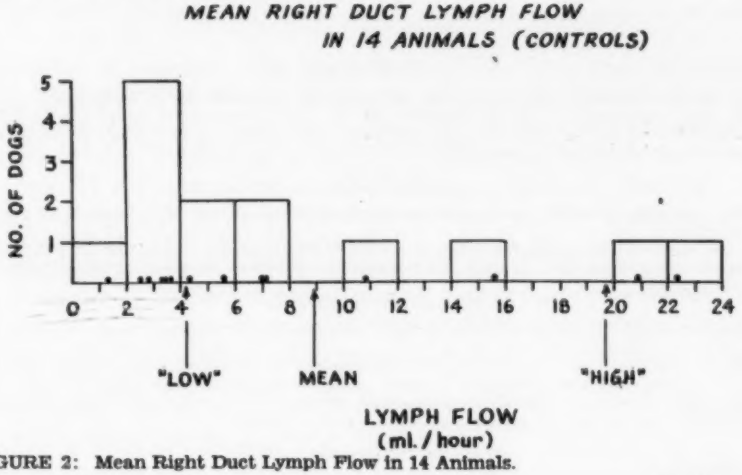

FIGURE 2: Mean Right Duct Lymph Flow in 14 Animals.

RIGHT DUCT LYMPH FLOW	MEAN	S.D.	RANGE	NO. OF DOGS
TOTAL FLOW	8.9 ml/hr .38 ml/kg/hr	± 8.1 ± .34	.8 - 35.0 ml/hr .01 - 1.3 ml/kg/hr	14
"LOW FLOW"	4.2 ml/hr .19 ml/kg/hr	± 2.2 ± .11	< 10 ml/hr < .5 ml/kg/hr	10
"HIGH FLOW"	19.7 ml/hr .88 ml/kg/hr	± 6.7 ± .22	> 10 ml/hr > .5 ml/kg/hr	4

FIGURE 3: Summary of the Right Duct Lymph Flows.

*Although the right duct lymph is principally from the lungs, lymph from other areas (cervical and subclavian) may contribute to the total flow.

Results and Discussion

Using conventional methods of cannulation, Drinker obtained right duct flow in approximately 20 per cent of dogs attempted.[4] Using the artificial chamber technique described, 15 successful collections of right duct lymph were made in 20 attempts (75 per cent success).

Figure 2 represents the distribution of mean hourly right duct flows in 14 dogs. The bars indicate the number of hourly flows lying within a given 2 ml. range. It is apparent that flows tend to occur in 2 groups, a "low" and a scattered "high flow" group.

Figure 3 summarizes the recording of the right duct flow. The mean flow is 8.9 ml./hr., however, if the flows are divided into "low" and "high" groups as suggested by the distribution curves, the majority of dogs (10) fall in the "low flow" group which averages 4.2 ml./hr. On the other hand, high flows (averaging 19.7 ml./hr.) were obtained in four dogs. It was noted that half of the "high flow" animals had cloudy lymph strongly suggesting that high flows were due to thoracic duct to right duct shunts and that the flows represented "pure" right duct flows. These figures are higher than those obtained by Warren and Drinker[1] (1.1 ml./hr., and Courtice,[5] 2.3 ml./hr., using conventional cannulation of single lymph channels).

SUMMARY

1. A new method for obtaining right duct lymph in the dog has been described.
2. The mean right duct flow was 4.2 ml./hr. and the presence of higher flows was (mean 19.7 ml./hr.) considered presumptive evidence of thoracic to right duct shunts.

ACKNOWLEDGMENT: The authors wish to express their thanks to Dr. William C. Voorsanger for his assistance in initiating these studies.

RESUMEN

1. Se ha descrito un método nuevo de obtener linfa del ducto derecho del perro.
2. El flujo promedio del ducto derecho, fué de 4.2 ml/hora y la presencia de flujos más copiosos fué (promedio 19.7 ml/hora) considerado como presunción de que existían intercomunicaciones entre los ductos derecho y torácico.

RESUMÉ

1. Une nouvelle méthode pour trouver un canal lymphatique droit chez le chien est décrite.
2. Le faible débit du canal droit fut de 4,2 mml. par heure et l'existence de débits plus élevés (19,7 mml. par heure) fut considérée comme une présomption de shunts thoraciques.

ZUSAMMENFASSUNG

1. Beschreibung einer neuen Methode zur Darstellung des rechten Ductus Lymphaticus beim Hund.
2. Die durchschnittliche Strömungsgeschwindigkeit im rechten Ductus betrug 4,2 ccm pro Stunde und das Vorliegen höherer Geschwindigkeiten (im Durchschnitt 19,7 ccm pro Stunde) wurde als mutmassliche Evidenz für einen Kurzschluss zwischen Ductus Thorazikus und rechtem Lymphgang angesehen.

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Inhalation and Skin Test in the Diagnosis of Asthma Bronchiale*

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The practical value of the skin test as diagnostic procedure in the study of bronchial asthma is regarded by various investigators quite differently. In the Scandinavian literature, for example, the skin tests are considered by Bruun[1] as a worthful aid in determining the allergenic factors responsible for asthmatic attacks. Kallner[2] is, on the contrary, of the opinion that cutaneous tests are of no practical importance. He points out that skin tests in a great number of cases give an incorrect positive result and in a sizeable number of cases a false negative one.

Friedewald[3] has published a survey of 1865 skin tests performed in 1900 allergic subjects. According to his opinion, they are of valuable help in the study of allergic diseases. Efron and Penfound[4] underline that patients suffering from seasonal hay fever have frequently absolutely negative skin reaction with the causative allergenic factor and many persons get a positive skin reaction having no clinical sign of an allergic disease. According to Unger[5] the skin tests give correct results in about 75 per cent of all cases of asthma bronchiale. Vaughan[6] explains the discrepancy between skin reactions and clinical manifestation of allergy with observations that a positive skin reaction may be an indicator of a present sensitivity, one that may develop in the future or it may be a tombstone for sensitivity in the past. Positive skin reactions particularly to some pollen may be of long duration. Vaughan has also observed that in some cases the patient may exhibit clinical signs of allergic disease before the skin test turns out to be positive. On the other hand, one may develop a positive skin reaction first and the manifest disease later.

In order to obtain more reliable results than the skin test is able to deliver, other methods of investigation have been tried. Stevens[7] has published a survey in which he compared the cutaneous sensitivity with pulmonary reactions to the nebulized allergens inhaled. However, Stevens did not include tests to pollens. Eleven of 45 patients tested had completely negative skin and inhalation tests. The remaining 34 patients were dermally sensitive to some of the allergens used. Fifteen of them reacted positively to one or more inhalation tests, developing symptoms of asthma. Stevens observed a positive inhalation test ten times where the skin failed to react. Lowell and Schiller[8] carried out inhalation tests with 75 asthmatic patients from six to 62 years old, using 5 per cent extracts of birch, oak, timothy and ragweed pollens, mold, alternaria and hormodendrum. House dust extract was used in concentration 1:400. A reduction of vital capacity of at least 10 per cent and/or a clearcut slowing in the rate of expiration, accompanied in several cases by physical signs of asthma was considered to be significant to presence of bron-

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chial or pulmonary sensitivity to the substance inhaled. Of the 75 patients tested, 57 reacted to one or several allergens. The writers mention that the incidence of positive skin reactions is more frequent than the number of reactions to inhalation test. They succeeded in producing a pulmonary reaction in no case when there was no reaction to the skin test with the allergen concerned.

Herxheimer[9] used for inhalation tests a nebulizer connected to a spirometer. He found, like Lowell and Schiller[8,10] a decrease of the vital capacity to be indicative of bronchial sensitivity. According to Herxheimer the inhalation test is superior to the skin test. Thus, he is of the same opinion as Lowell and Schiller who regard the inhalation test to be a more valuable method for determining the causative inhalants in bronchial asthma. Herxheimer has used inhalation of small quantities of nebulized allergen extracts also for therapeutic purposes, for hyposensibilization. Stronger allergen concentrations lead, on the contrary, to hypersensibilization.

Arner[11] observed and measured decrease of the relative oxygen tension in asthmatics who reacted to inhalation of nebulized allergen extracts. Colldahl,[12,13] who also considers the skin test to have a certain importance in diagnosis of bronchial asthma, received a positive result in inhalation test in 43 per cent of patients who gave a positive skin test with the allergen concerned. Furthermore, 16 per cent of asthmatics with a negative skin test reacted positively to inhalation test performed with the same substance. These experiences were gained in a material of 44 patients, whereby 169 inhalation tests were carried out.

In the lung medicine department of Eksjö Sanatorium, asthmatic patients have been taken care of since 1956. Since March, 1957, we have tested them regularly by the inhalation as well as the intracutaneous method.

Allergenic extracts diluted with Coca's solution, produced by firma Vitrum in Stockholm are used for both tests. In patients who react with asthmatic symptoms to inhalation of plain Coca's solution (we have observed five cases), extracts made with normal saline can be used. The intracutaneous tests have been performed usually in concentration of 1:1000. In some cases, however, in concentration of 1:10 000 or 1:100 000. 0,02 ml. of the solution has been used for a single injection, the results being determined 15 minutes after injection.

We consider an inhalation test performed directly with a substance concerned as a very dangerous one. Therefore, we use only allergenic extracts in various concentrations. The strongest concentration we ever use is — 1:10. Usually, we begin with concentration of 1:1000. When — according to the medical history or a strongly positive skin test — sensitivity of a considerable degree can be suspected we have begun inhalation tests with weaker concentrations, 1:10 000 or 1:100 000. If necessary, the testing extract can be diluted even more.

The same principle — working with weaker concentrations, if this is regarded as necessary — also applies for intradermal tests. When testing children and in cases when strong sensitivity is suspected we perform

intracutaneous tests with concentrations of 1: 10 000 or 1: 100 000, using only 10 or 15 allergenic extracts in one session. Positive skin reactions have been indicated with + to ++++, compared to the size of the infiltrate produced by intracutaneous injection of 0,02 ml. histamine solution in concentration 1:10 000, reaction to this being registered with +++. Coca's solution served as the controle for a negative reaction.

The inhalation tests have been carried out with help of Pari-Optimal membrane compressor-nebulizer (Paul Ritzau Pari-Werk, Starnberg am See/Obb., Germany), aerosolized Vitrum's allergenic extracts in concentration from 1:100 000 to 1:10 being used as testing substances. Before starting inhalation tests, patients should be free from subjective and objective symptoms of asthma. Furthermore, approximately a week previously, steroid, aminophylline or ephedrine treatment should be discontinued.

The results of inhalation tests are determined by auscultatory findings. Appearance of sibilant rhonchi during the first five inhalations is indicated as a +++ reaction, within 15 breaths with ++ and after this, the reaction is indicated with +. We have used up to 1 ml. of each concentration. This amount is sufficient for about 30 breaths. We consider the determination of a reaction according to clinical and subjective symptoms of asthma as sufficient and regard the measurement of vital capacity or other methods of registration of a positive inhalation test as unnecessary. We have, however, in a number of cases followed the count of eosinophil cells in blood smear after inhalation tests. There is some evidence that the eosinophilic count has a tendency to increase in connection with a positive reaction, in extreme cases up to 20 per cent or more (Kaude). We have not observed complications or severe reactions in patients tested according to the method prescribed. It is, however, important to perform inhalations carefully and observe the patient some time afterwards. A patient usually reacts within 10 - 15 minutes, in a few instances as late as a couple of hours after inhaling the aerosolized allergenic extract. It is often advisable, to relieve an induced reaction by inhaling nebulized isoprenaline, isopropydrine etc., as soon as a positive reaction has been verified. Usually symptoms fade within some minutes. Only in a few cases has it been necessary to treat patients with aminophylline or steroids in small amounts.

Ingestad[15] published in 1957 a preliminary report on inhalation tests performed in 56 asthmatic patients treated in Eksjö Sanatorium. He could point out ten asthmatics who gave a negative skin test, but reacted positively to inhalation of aerosolized allergenic extracts. To six of these patients 0,1 ml. of the extract in question in concentration 1:100 or 1:10 was injected intracutaneously. Four of them responded to this injection with asthmatic symptoms, but developed no skin reaction in spite of the strong allergen concentration.

By July 15, 1958, the total number of inhalation tests performed on 200 asthmatic subjects from eight to 72 years old was over 1000. In selection of testing substances the medical history of each patient and partly the positive skin reactions have been taken into consideration.

TABLE 1

Allergen	Correspondence: Pos. skin and pos. inhal. test	Correspondence: Neg. skin, and neg. inh. test	Discrepancy: Pos. skin, Neg. inh. test	Discrepancy: Neg. skin, pos. inh. test	Total number of inhalation tests performed
Cotton	1	7	1	1	10
House dust	12	72	21	17	122
Horsehair	0	49	2	12	63
Feathers	2	75	3	12	92
Sheep's wool	8	41	7	20	76
Excelsior	1	14	2	5	22
Dog epithel	4	25	8	7	44
Horse epithel	20	18	18	4	60
Cat epithel	5	17	5	1	28
Cow epithel	14	10	27	5	56
Swine epithel	3	6	9	1	19
Mould	7	46	27	13	93
Pollens					
Dandelion	2	4	3	0	9
Ox-eye daisy	3	42	15	7	67
Rye	1	5	4	0	10
Timothy	7	46	8	11	72
Oak	1	0	2	2	5
Alder	0	0	3	1	4
Birch	1	9	2	1	13
Hazel	0	1	3	1	5
Elm	1	3	3	0	7
Aspen	0	1	3	1	5
Sallon	1	0	5	1	7
Reed	3	8	12	1	24
Heather	1	1	4	0	6
Rape	2	8	4	0	14
Fir	1	9	4	3	17
Pine	4	7	6	4	21
Mixed tree[1]	5	54	8	17	84
"Auto" house dust[2]	1	6	3	5	15
					1070

[1]Containing four pollens: Oak, alder, birch and hazel pollen
[2]Prepared from patient's own house dust.

TABLE 2

Allergen groups	Correspondence: Pos. skin and pos. inhal. test	Correspondence: Neg. skin and neg. inhal. test	Discrepancy: Pos. skin and neg. inhal. test	Discrepancy: Neg. skin and pos. inhal. test	Total number of inhalation tests performed
	No. = Per cent	No. = Per cent	No. = Per cent	No. = Per cent	
Pollens	33 = 9	198 = 53.5	89 = 24	50 = 13.5	370
Animal epithel	54 = 19	117 = 41.5	74 = 26	38 = 13.5	283
Mould	7 = 7.5	46 = 49.5	27 = 29	13 = 14	93
House dust	13 = 9	78 = 57	24 = 18	22 = 16	137
Others (cotton, horsehair, feathers, excelsior)	4 = 2	145 = 78	8 = 4	30 = 16	187
Totally	111 = 10	584 = 54.5	222 = 21	153 = 14.5	1070

TABLE 3

	Number of Positive skin tests	Positive inhalation tests		Negative inhalation tests	
		No.	Per cent	No.	Per cent
Pollens	122	33	= 27	89	= 73
Animal ep.	128	54	= 42	74	= 58
Mould	34	7	= 19	27	= 81
House dust	37	13	= 35	24	= 65
Others	12	4	= 33	8	= 67
Totally	333	111	= 33⅓	222	= 66⅔

Thus, the inhalation tests are limited to a certain number of allergens. A general survey of inhalation tests performed with various aerosolized allergenic extracts is given in Table 1. The results are divided into two groups: those in which the skin and inhalation test agree and those in which they differ. Allergens used in a small number of cases and five pulmonary reactions to Coca's solution (skin control being negative in all five patients) as well as those tested only for dermal reactions, are not included.

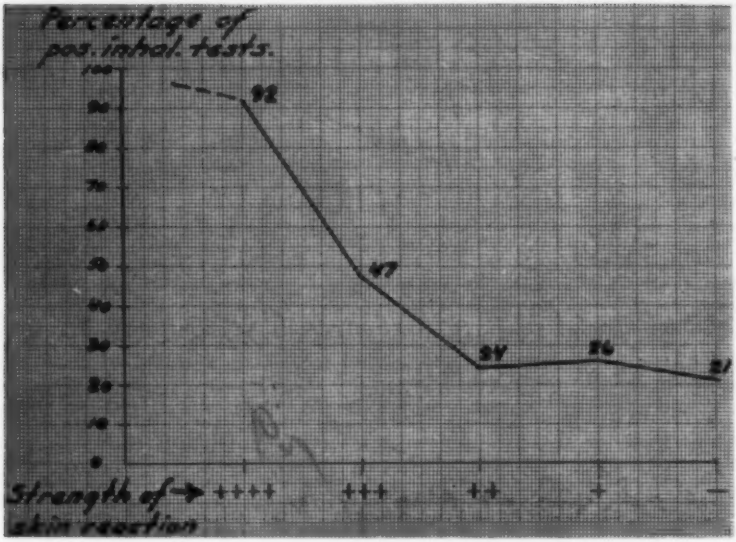
In Table 2, the allergens are divided into five groups: pollens, animal epithel, mould, house dust and another "house group," including cotton, horse hair, feathers and excelsior. Dealing with these larger groups we can better compare the relations between skin and inhalation tests. The highest coincidence of positive dermal and pulmonary reactions is present in the animal hair group with 19 per cent. Totally, there is a discrepancy between dermal and pulmonary sensitivity in 35.5 per cent. That means, in more than ⅓ of all cases the skin test — negative or positive — does not give reliable results.

Table 3 reveals some interesting experiences. The inhalation tests are based on positive skin tests. We see that in only 33⅓ per cent of the cases inhalation test turned out to be positive and in 66⅔ per cent of the cases skin test gave positive results to allergens which did not induce asthmatic reaction in inhalation test.

The highest coincidence — 42 per cent — in dermal and pulmonary sensitivity could be observed in the animal hair group. Positive skin

TABLE 4

	Number of Negative skin tests	Positive inhalation tests		Negative inhalation tests	
		No.	Per cent	No.	Per cent
Pollens	248	50	= 20	198	= 80
Animal ep.	155	38	= 24.5	117	= 75.5
Mould	59	13	= 22	46	= 78
House dust	100	22	= 22	78	= 78
Others	175	30	= 17	115	= 83
Totally	737	153	= 21	584	= 79



reactions, performed with mould extract gave reliable results only in 19 per cent.

Table 4 shows that in between 17 and 24.5 per cent of negative skin tests the asthmatic subject may react positively to inhalation of the aerosolized allergen concerned. Thus, in the average of 21 per cent, the extract up to the concentration of 1:1000 of the substance that is able to induce a pulmonary reaction in asthmatics fails to give slightest local reaction when administered intracutaneously.

The relation between the strength of dermal sensitivity and the positive results in inhalation tests is shown in Fig. 1. In cases, both tests have been carried out, the skin reaction being strongly positive, the inhalation test turns out to be positive in 92 per cent. In presence of milder skin reactions a positive result in inhalation test can be expected in only about 25 per cent, in spite of the fact that medical history for performing inhalation tests has been taken into consideration in a higher degree than in strongly positive skin reactions.

In our series of 200 asthmatic patients with 1070 inhalation tests performed according to medical history and positive skin tests, we failed to find any positive pulmonary reaction in 44 patients, or about 20 per cent of the cases. Thus, in 80 per cent of our material we were able to determine one or more exogenous factors that caused patient's sickness with great probability. According to Feinberg and Feinberg,[16] in about 30 to 50 per cent of allergic cases the causative agent cannot be determined. We are of the opinion that this figure can be considerably reduced when the inhalation test is regularly used in the investigation of bronchial asthma.

SUMMARY

The inhalation test is a valuable investigation method in diagnosis of bronchial asthma. It can be carried out simply and safely, its results being superior to those of skin tests. Observations based upon 1070 inhalation tests in 200 asthmatics showed

that dermal sensitivity corresponds to pulmonary sensitivity only in ⅓ of cases with positive skin tests. However, in presence of strong skin reactions the incidence of positive inhalation tests is high. Milder skin reactions are less valuable in selection of allergens for performance of inhalation tests. The highest coincidence in positive skin and pulmonary reactions was found in tests with animal hair extracts. In cases of negative skin test the allergen concerned may induce a positive inhalation test in approximately 21 per cent.

RESUMEN

La prueba de la inhalación es un método valioso para el diagnóstico del asma bronquial. Puede llevarse a cabo sencillamente y con seguridad. Sus resultados son superiores a la prueba cutánea.

Las observaciones basadas en 1,070 pruebas de inhalación en 200 asmáticos, demostraron que la sensibilidad dérmica corresponde a la sensibilidad pulmonar sólo en ⅓ de los casos con pruebas cutáneas positivas.

Sin embargo, en presencia de fuertes reacciones cutáneas, la incidencia de positivas por inhalación es elevada. Las reacciones cutáneas moderadas son de menos valor en la selección de los alérgenos para llevar a cabo las pruebas de inhalación.

La más elevada coincidencia de reacciones cutáneas positivas y reacciones pulmonares se encontró en las pruebas con pelo de animales en extracto. En los casos de reacciones cutánea negativa el alérgeno correspondiente puede producir una prueba positiva de inhalación en aproximadamente el 21 por ciento.

RESUMÉ

Le test par inhalation est une méthode d'investigation valable dans le diagnostic dé l'asthme bronchique. Il peut être pratiqué simplement et sans danger, ses résultats étant supérieurs à ceux des tests cutanés. Des observations basées sur 1.070 tests par inhalation chez 200 asthmatiques montrèrent que la sensibilité du derme correspond à la sensibilité pulmonaire seulement dans ⅓ des cas décelés par tests cutanés positifs. Cependant, en présence de réactions cutanées fortes, la fréquence des tests par inhalation positifs est élevée. Des réactions cutanées plus faibles sont moins valables dans la sélection des allergènes pour la pratique des tests par inhalation. La coincidence la plus élevée dans les réactions positives cutanées et pulmonaires fut trouvée dans les tests avec extraits de poils d'animaux. Dans les cas de test cutané négatif, l'allergène en cause peut produire un test par inhalation positif dans environ 21%.

ZUSAMMENFASSUNG

Der Inhalationstest ist eine wertvolle Untersuchungsmethode bei der Diagnose des Bronchialasthmas. Er kann leicht und sicher ausgeführt werden, und seine Ergebnisse sind denen, die mittels Hauttest gewonnen wurden, überlegen. Die sich auf 1070 Inhalationsteste bei 200 Asthmapatienten stützenden Beobachtungen zeigten, dass die Hautempfindlichkeit der Lungenempfindlichkeit nur in einem Drittel der Fälle mit positivem Hauttest entspricht. Jedoch sind bei Vorliegen starker Hautreaktionen positive Inhalationsteste sehr häufig. Schwächere Hautreaktionen sind von geringerem Wert bei der Auswahl von Allergenen zur Durchführung von Inhalationstesten. Das häufigste Zusammentreffen von positivem Haut- und positivem Lungentest fanden wir bei Proben mit Tierhaarextrakten. In Fällen mit negativen Hautproben vermag das betreffende Allergen in ungefähr 21% zu einem positiven Inhalationstest zu führen.

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SECTION ON CARDIOVASCULAR DISEASES

The Complete Relief of Mitral Stenosis: Ten Years of Progress Toward This Goal

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PART I

(This article is being published in two parts.
Part II will appear in the June issue of this Journal)

Mitral stenosis, being basically a mechanical lesion, logically might be expected to lend itself to correction by surgery which is the mechanical arm of therapeutics. Surgical procedures for mitral stenosis are, in fact, being practiced widely by many surgeons throughout the world and the accumulated experience with this operation is extensive. It is nothing short of surprising, therefore, that many patients with mitral stenosis are being carefully kept away, frequently by most competent cardiologists, from the opportunity for surgical relief. Might it not be that many cardiologists are disenchanted, to a certain extent, with the results of the accepted surgical procedure (whichever name is given to it — mitral commissurotomy, valvotomy, valvulotomy, valvuloplasty) which is performed for mitral stenosis?

The dissatisfaction of many prominent surgeons with the established surgical techniques is not a matter for conjecture. In a recent international inquiry (under the auspices of the American College of Chest Physicians) among surgeons with extensive experience in this field (10,000 cases in aggregate) 50 per cent of those who responded expressed dissatisfaction with existing surgical procedures.[1]

The impression is clearly gained that surgery for mitral stenosis, as generally practiced, must be wanting in certain important respects. It may be profitable, therefore, to re-examine the therapeutic concepts which underlie the accepted surgical procedure for stenosis of the mitral valve.

As far back as 1898, Samways[2] proposed that the stenotic mitral valve be enlarged surgically. Brunton in 1902[3] even went so far as to urge that this enlargement be accomplished by "lengthening the mitral slit." Bold and logical as these suggestions were, a quarter of a century passed

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before any serious surgical attempts in this direction actually were made. Even then, the objective of the surgical pioneers of the 1920's was, in the main, to find a safe surgical approach for manipulations within the interior of the functioning heart. The actual surgical enlargement of the stenotic valve opening did not appear to pose a serious problem. After all, the surgical relief of stenotic lesions in other parts of the body by comparatively simple surgical maneuvers was well established. Not until the late 1940's, when (as the result of the perfection of endotracheal anesthesia, the availability of blood replacement, and the development of antibiotic drugs) the "cardiac barrier" was finally passed, did it become painfully apparent that the existing surgical experience with correction of stenotic lesions in other parts of the body could not be translated in unmodified fashion to the relief of stenosis of the heart valves. Enlargement of the valve orifice by the removal of obstructing valve tissue with the aid of a punch[4] produced serious and often fatal regurgitation. The concept of "selective insufficiency," proposed by Harken et al,[5] while sensing the importance of avoiding the creation of a major degree of regurgitation, did not offer a positive plan for the effective enlargement of the valve orifice without the production of incompetence. The introduction by Bailey[6] in 1948, of the

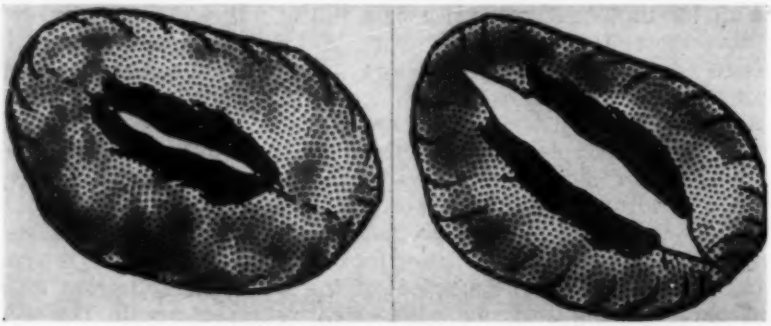

FIGURE 1: Original concept of division of commissures of stenotic mitral valve. It was presumed that functional mobility would be restored to both "leaflets." Bailey, C. P. Glover, R. P., and O'Neill, J. T., Jr. Courtesy of *J. Int. Coll. Surg.*, 13:4, 1950.

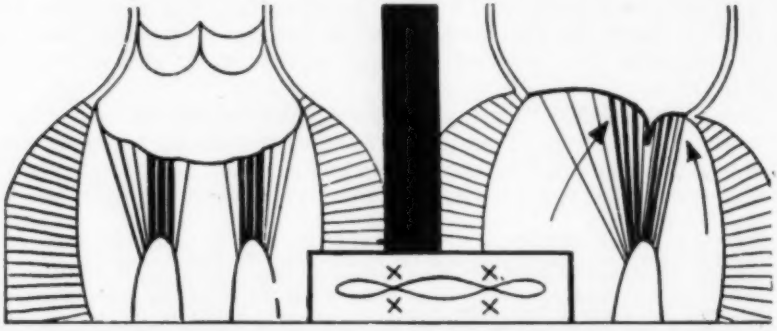

FIGURE 2: Schematic representation of mitral valve as visualized by Brock, R. C.: Surgical and Pathological Anatomy of the Mitral Valve, Courtesy of *Brit. Heart Journal*, 14:489, 1952.

concept of enlargement of the stenotic mitral valve by division of the valvular "commissures," leaving chordal attachments on both sides of the division, may be considered the major contribution which led to the actual "breakthrough" in the surgical treatment of mitral stenosis (Fig. 1). The surgical concept which thus achieved recognition and acceptance for all valvular lesions of the heart required that the relief of stenosis of a heart valve be accomplished without interference with the competence of the valve mechanism. All of the procedures which are commonly practiced today for the surgical relief of mitral stenosis (commissurotomy, valvotomy, valvulotomy, valvuloplasty) are based upon this principle. The description by Brock in 1952[7] of the anatomical and pathological factors underlying the commissural concept helped to strengthen its position as the basis for the surgical treatment of this lesion. The mitral valve was visualized by Brock as composed of two apposing leaflets which make contact during systole along a central line as the result of their respective movement toward one another (Fig. 2). Stenosis of the valve was attributed to crossfusion of the valve leaflets, particular stress being placed by Brock upon two specifically described points of contact. Satisfactory surgical separation of these crossfused areas, involving simple though complete division of this presumed line of fusion, including the specially described points of contact, therefore, should result in the restoration of free movement to both valve leaflets.

The commissural concept, particularly as described by Brock, apparently provided the blueprint for essentially complete restitution of function to the stenotic mitral valve.

With the theoretical basis thus firmly laid, it remained for the operating surgeon to achieve in practice the nearest approximation to the ideal technical mobilization feasible in each individual case.

FIGURE 3: Refusion of the originally widely opened anterolateral commissure demonstrated at autopsy in R. S. a 42 year old white woman six and one half years after operation.

Unfortunately, however, this did not prove so simple. Surgical division of the so-called "posteromedial commissure," in the projected linear fashion, frequently resulted in a considerable degree of mitral regurgitation, and Bailey, as well as other surgeons as the result of early experience, suggested that surgical efforts be concentrated mainly at the "safer" anterolateral commissure. With increasing experience and reorientation as to the direction of the line of the posteromedial commissure, however, both commissures have become more amenable to effective surgical division in more recent years. The development of various types of valvulotomes and the introduction of the bare finger technique helped further to improve the surgical accomplishments. The recognition of the importance of subvalvular stenosis (chordo-papillary agglutination) by Harken and Black[8] and surgical maneuvers recommended for it by Nichols and Jamison[9] provided another step in the effective surgical relief of the stenotic mitral valve.

The combination of a simple concept which apparently offered a theoretical basis for the complete surgical restitution of the mitral valve, together with the important technical improvements mentioned above, and the skill born of continuing experience might have been expected to provide excellent results in a high proportion of cases.

Results of Mitral Commissurotomy

Never in the history of modern surgery has a completely new major surgical procedure been performed by so many surgeons in such large numbers in such a short period as has been the case with mitral commissurotomy (used as a generic name to include also the identical techniques of valvulotomy, valvuloplasty, valvotomy). As the result of this extensive experience we have been able to gain, unusually early in the

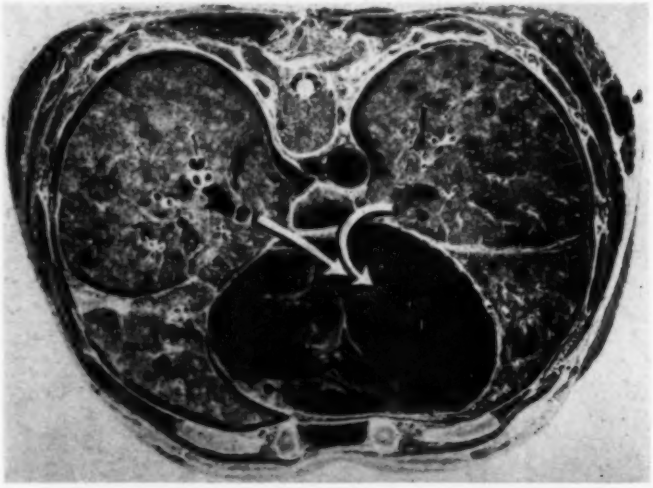

FIGURE 4: Cross-section of human thorax at the level of the mitral valve. Note the line of direction of the atrioventricular canal and the enhanced facility with which the valve may be approached by way of the right thoracic cavity. Courtesy of Prof. P. Seara, "Estudio Anatomico Topografico Del Torax y Del Abdomen" Buenos Aires, Argentina, 1956.

development of this operation, a clearer perspective with regard to its effectiveness, its complications, and its risks.

The published data from large individual series of mitral commissurotomy operations[10] and from more modestly sized,[11,12] although probably more significant, follow-up studies, as well as the data from the international inquiry (made under the auspices of the American College of Chest Physicians) which comprised 10,000 surgical cases from 37 clinics,[1] blend into an essentially uniform picture of the achievements and limitations of this operation. These may be summarized as follows:

1. Mitral commissurotomy does consistently produce definite and immediate amelioration of symptoms in a large proportion of patients. Since such subjective improvement is dependent to a very marked degree upon the patient's self-appraisal it is not surprising that the statistics of different clinics vary considerably.

In a late follow-up study by Likoff et al[11] of 200 patients operated upon at our clinic between 1948 and 1952, 55 per cent were either markedly or moderately improved five to eight years after the operation. In a study by Otto et al of 106 cases followed one to five years after operation[12] improvement was reported in 77 per cent of the surviving patients.

In the international inquiry mentioned earlier,[1] the experience of 34 clinics with 5,482 patients demonstrating the early results (six months) and in a smaller number of patients (342) the late results (five years) are presented in Table 1.

2. The objective physical signs of mitral stenosis, particularly with regard to auscultatory findings, remain essentially unchanged in the great majority of patients following commissurotomy. The typical diastolic murmur, disappears in only 8 to 10 per cent of operated cases.

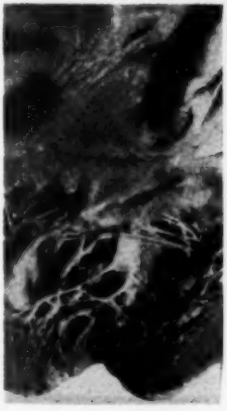

Figure 5A

Figure 5B

FIGURE 5A: Localization of the subaortic curtain (between dotted lines which indicate adjacent aortic attachment of noncoronary and left coronary aortic valve cusps). Note that it is directly continuous with the so-called "septal leaflet" of the mitral valve.

FIGURE 5B: Photograph of a normal mitral valve (atrial aspect) showing arcuate line of closure, delicate marginal convolutions, and line of "horse-she" shaped annulus fibrosus (dotted line) with its trigonal terminations. Bailey et al, Courtesy of *Advances in Cardiology*, Editor: Prof. R. Hegglin. (S. Karger Ltd. Basle, Switzerland, 1959).

There is more frequently a quantitative improvement in some of the signs which indicate the severity of the stenosis (the high pitched first sound) or the pulmonary hypertension (pulmonary second sound).

On the whole, however, the criteria by which the clinical diagnosis of mitral stenosis is usually made are still present in most of these patients after commissurotomy.

3. Pre and post-operative cardiac catheterization studies usually indicate demonstrable improvement in the physiological derangement produced by the obstruction at the mitral valve. The complete study of Dickens et al[28] combined (right and left) heart catheterization of patients who underwent mitral commissurotomy — showed definite improvement in terms of a significant reduction in the pressure gradient across the mitral valve together with a satisfactory increase of cardiac output in 9 of 16 patients. Less significant physiological improvements were found in some of the other patients. These data go hand-in-hand with the symptomatic improvement usually observed, although they do not indicate the complete disappearance of physiologically significant stenosis since they are performed under conditions of rest. Under conditions of exertion either slight or more severe it is quite possible (even probable) that the physiological findings in these cases might again become grossly abnormal.

FIGURE 6: The ventricular aspect of the normal mitral valve showing its continuous cylindrical or "sleeve-like" structure. There is no true division into leaflets as is implied by the term "bicuspid valve." The base of the "cylinder" is obliquely truncated thus rendering the septal portion (A) considerably longer than the mural portion (B). Bailey et al, Courtesy of *N. Y. State J. Med.* 56:653, 1956.

4. Recurrence of tight mitral stenosis after an initially satisfactory mitral commissurotomy definitely does occur, (Fig. 3) though there exist considerable differences of opinion regarding its frequency. Ellis and Harken[14] described only one patient in a series of 500 in whom refusion across the surgically divided commissures could be demonstrated at autopsy although more recently[16] they have conceded the possibility of a higher incidence of this complication. Glover et al,[15] too, considered restenosis a rarity. Many other surgeons, however, even in these few years have encountered the condition with increasing frequency. Among 8638 cases reported by 31 surgeons (American College of Chest Physicians report[1] recurrence of mitral stenosis after commissurotomy had already been demonstrated in 2.8 per cent of patients and the opinions expressed by these surgeons indicated that they expect this percentage to rise significantly.

Indeed, of those patients who were operated at our clinic before the end of 1952, 12 per cent already have been reoperated for recurrence of the mitral obstruction. It is our considered opinion that with the passage of the years recurrence of mitral obstruction either due to

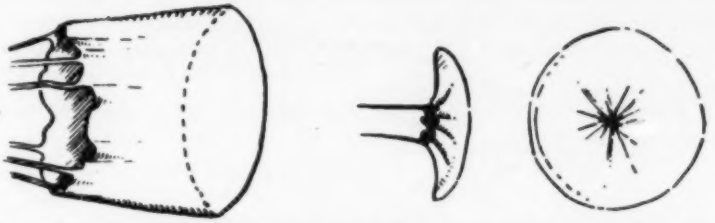

FIGURE 7A: Diagrammatic demonstration of the mechanism of action of a symmetrical sleeve valve with flexibility and support comparable to that of the mitral valve. At full opening (diastole) a passage of maximal caliber is provided. On closure (systole) the flexible wall falls in from all sides to approximate at a central point.

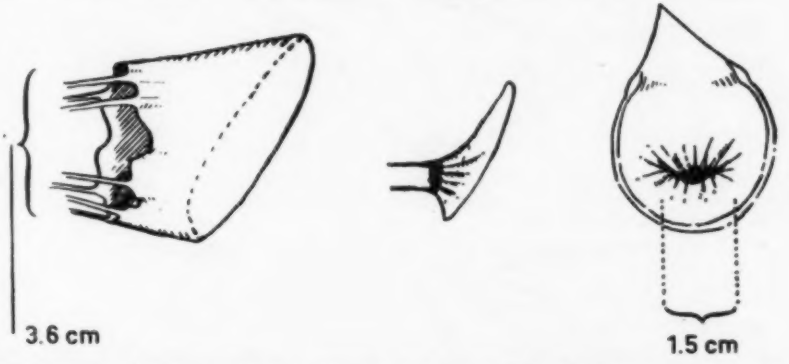

FIGURE 7B: With an obliquely truncated sleeve such as the mitral valve the total hydraulic pressure effective upon the longer or septal side during systole is considerably greater than that upon the shorter (mural). Therefore, the line of closure necessarily becomes arcuate. In mitral stenosis the valve apex not only becomes "purse-stringed" but often tends to become "frozen" in this position of closure. The linear measurements shown here are hypothetical but are in proportion and illustrate clearly that even an ideal separation of fused commissures is incapable of restoring a passageway of normal calibre unless the valve edge is thin and capable of unfolding to its diastolic position (See Fig. 9 AB).

orificial narrowing or to marginal hardening (Fig. 3) may be expected in practically every surviving patient in whom the older type of procedure was performed unless it was complicated by the existence or creation of insufficiency, or unless the valvular separation happened to become extended, inadvertently, considerably beyond the limits of valvular scarring or commissure formation.

5. Mitral commissurotomy is performed at a risk of an operative mortality which, though not considered forbidding for so disabling a condition as mitral stenosis, is markedly higher than is appreciated generally. Notwithstanding the important advances which have been made in the technique of this operation, the over-all mortality has not been reduced significantly. For the 10,000 operations reported by 37 clinics in the international inquiry mentioned,[1] the over-all operative mortality was 6.8 per cent. Similar figures are reported in several large individual series. From the studies of Ellis, Harken, et al,[10] the impression is gained that the operative mortality of mitral commissurotomy is practically completely limited to patients presenting themselves in the final stages of the disease. However, they report[10] only 913 survivors following 1000 operations for mitral stenosis which represents an

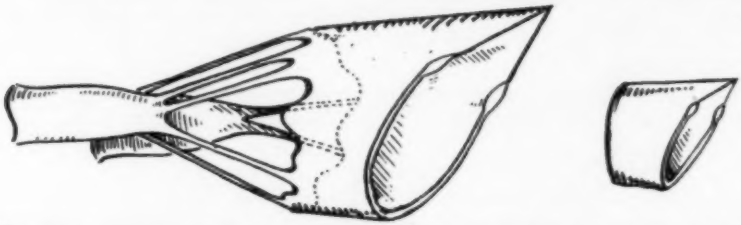

FIGURE 8A: Diagrammatic representation of the normal mitral valve "cylinder" with its supporting structures.

FIGURE 8B: The maximal effect of the rheumatic inflammation is on the marginal portion of the valve sleeve, producing thickening and fibrosis of a periorificial zone of about one centimeter in width.

FIGURE 8C: The contracture of healing of the tissue in this inflamed zone brings about a "purse-stringing" of the free margin of the valve "cylinder" which thereby becomes converted roughly into a valve "cone." The chordae and papillary muscles partake of this inflammation to a variable degree. Bailey et al, Courtesy of *Advances in Cardiology*, Editor: Prof. R. Hegglin. (S. Karger Ltd. Basle, Switzerland, 1959).

over-all mortality of 8.7 per cent, a figure which is not dissimilar to that of other clinics. In our own experience which by now includes well over 2,500 cases, there exists a not insignificant mortality risk even in Class II* (about 2.4 per cent). As the patient's functional class becomes worse, the mortality increases in proportion (9.2 per cent for Class III and 18 for Class IV). Our over-all mortality for 1217 patients who underwent mitral commissurotomy (left sided procedure) from 1949 until 1955 was 7.9 per cent. It may be of interest to note that our over-all operative mortality from 1951 till 1955 has varied, annually, only between 8.2 and 5.8 per cent. Since operative mortality in mitral stenosis is related definitely to the functional status of the patient, the comparatively slight variation in the annual over-all mortality is a reflection of the fact that the proportion of Class II and Class III patients (together about 94 per cent of all patients) who come to our clinic for surgical relief has remained approximately the same over the years.

6. An additional risk of mitral commissurotomy is expressed in the incidence of serious complications and chronic morbidity which may result from the surgical intervention, especially arterial embolization and the creation of physiologically significant mitral insufficiency. As Table II indicates, arterial embolization accounts not only for a significant part of the operative mortality but also detracts from the sum of satisfactory results in the survivors.

The same applies to mitral insufficiency created at time of operation. Such a complication may leave the patient not only unimproved but actually worse off than before operation.

*New York Heart Association Classification

Figure 9A

Figure 9B

FIGURE 9A: Diagrammatic representation of atrial aspect of stenotic mitral valve with extensive cross-fusion of the flattened apex thus forming the commissures. Note the extensive involvement of shorter mural portion of the valve. While the septal portion is involved for an equally great distance, because of its greater length, its basal tissue remains flexible and grossly normal.

FIGURE 9B: Same as A after performance of the older (commissurotomy) type of operation. It can be readily seen that this procedure is only capable of establishing a relatively rigid fissure-like opening of but limited size.

The only conclusion to which a careful evaluation of this wealth of data permits us to come is that, while mitral commissurotomy can and frequently does relieve the symptoms of mitral stenosis to a considerable extent, it seldom abolishes the clinical picture of mitral stenosis; nor does it often relieve completely the anatomical obstruction at the valve as expressed in terms of physiological data. This operation, therefore, can be looked upon only as a palliative procedure the improvements produced by which, though frequently considerable, are generally of an impermanent nature only. In addition, this improvement is gained at the expense of a not insignificant incidence of serious complications and an operative mortality which is still relatively high.

Toward a New Approach

The limitations of mitral commissurotomy result from the fact, of which many surgeons have become increasingly and painfully aware, that the actual opening achieved by splitting or incising the commissures usually falls far short of a true relief of the stenosis. Recently, some able surgeons[16] have advocated the use of powerful, mechanical, disruptive force in one fashion or another to achieve greater enlargement of the valve orifice. While such means undoubtedly may prove effective at times they necessarily carry the risk of rupturing the valve components and producing severe insufficiency. The application of blind disruptive force to the basically delicate tissues of a structure as important as a heart valve cannot be considered as anything but a step backward, an atavistic development which is reminiscent of the early attempts at relief to mitral stenosis without regard for the competence of the valvular mechanism.

Our dissatisfaction with the results of our own surgical experience in more than 1500 operated cases of isolated mitral stenosis in 1954 stimulated one of us (C. P. B.) to consider other possible surgical methods. The search was for a technique which would provide a more complete relief of the obstruction at the valve level and, thereby, improve the actual results as well as reduce the operative mortality. When the possibility of approaching the mitral valve from the right side by way of the dissected interatrial groove was recognized,[17] this anatomical avenue was explored with this objective in mind. It soon became apparent that the new approach permitted the performance of a much superior commissurotomy because of the more direct and efficient access to both commissures which it provides. The explanation lies in the fact that although the mitral valve is situated slightly to the left side of the body, its atrial aspect faces backwards, upwards, and to the right (Fig. 4). Hence, it may be reached via the dissected interatrial groove in a nearly straight line. By the usual left-sided transappendageal approach, in contradistinction, the valve can only be reached "around the corner," and all manipulations, therefore, are rendered more difficult and complicated, especially when instrumentation is required. Many other technical advantages of the right-sided approach soon became apparent. There is less likelihood of producing an extended tear in the atrial wall than when operating through the thin and often rather friable left auricular appendage. The right-sided approach also permits avoidance of the most common thrombus-bearing area—the left auricular appendage and ad-

jacent left atrial wall—and thus reduces considerably the operative risk of arterial embolization. But by far the most important contribution of the right-sided approach to the effective surgical relief of the stenotic mitral valve, arose from the fact that by permitting better surgical orientation and more deliberate manipulation of the valve, it provided conditions favorable for the evolvement of a completely new surgical concept for the relief of mitral stenosis. To satisfy some of our more classically trained colleagues, the procedure has been called "neostrophingic* mobilization of the mitral valve" although more properly it may be described as the "creation of a functional septal leaflet."[18] This concept does not aim at the mere enlargement of the stenotic orifice but at the establishment of an entirely new type of mechanism for the mitral valve which nearly invariably will have been mutilated irretrievably by the pathological process. By freeing up the longer septal portion of the valve a "flap" may be fashioned which thereafter hinges freely upon its flexible basal attachment. The success of this new principle in practice induced one of us (J. Z.) to re-examine the functional anatomy of the mitral valve with rather startling results.

Anatomy

The functional anatomy of the normal mitral valve,[19] as based upon a study of the fresh heart as well as of the functioning normal valve in the living organism, provides a completely different picture from the one commonly described in anatomical texts. The more important features relevant to surgery of the mitral valve involve the "annulus fibrosus" and the "valve leaflets."

*neo(Gr.) - "new;" strophings (Gr.) - "turning."

FIGURE 10: Photograph showing complex subvalvular "shortening" and cross-fusion of the chordae and papillary muscles. Such fusion masses attach directly to the valve apex and reinforce the primary stenosis which is due to the purse-stringing of the valve "cylinder."

When we refer to an annulus fibrosus of a heart valve we are wont to visualize a relatively fixed structure of fibrous tissue in the form of a complete ring which gives attachment to the valve substance. In actual fact, however, the only structure related to the mitral valve which might be called an "annulus fibrosus" is a horseshoe-shaped fibrous line of thickening of the upper edge of the posterior aspect of the left ventricular myocardium which extends from the right fibrous trigone on one side, to the left fibrous trigone on the other. The gap between these two points is bridged by a thin curtain-like structure which takes origin from the lower edge of the root of the aorta between the attachments of the left and the non-coronary aortic cusps. This curtain continues down to become what is usually described as the "septal leaflet" of the mitral valve (Fig. 5 AB). Only by stretching the term far beyond its usual meaning can we refer to an "annulus fibrosus" of the mitral valve.

A similar inaccuracy is involved in the classical description of the mitral valve in which it is visualized as composed of two ("bicuspid") or sometimes even more valve leaflets. The concept of mitral valve leaflets implies, by analogy with the aortic and pulmonic valve cusps which are discrete structures, the existence of similarly discrete mitral leaflets. No such discrete leaflets, however, can be demonstrated in the mitral valve. The normal mitral valve is a continuous membranous ribbon with an irregularly shaped edge hanging down obliquely from its attachment to the ventricular myocardium and the subaortic curtain in "wind-sock" or "sleeve" fashion (Fig. 6). The valve sleeve is longer anteriorly, customarily described as the "septal" or "aortic leaflet," shorter posteriorly ("mural leaflet") and shortest at the sides—the "junctional" areas. At its narrowest points the normal valve ribbon may measure as little as 4 to 5 mm. in length. Chordae tendinae are attached all along the free edge of the valve or in close proximity to it although certain chordae arise at a variable distance from the free margin of the valve sleeve.

From the above mentioned facts and from digital examination of the moving valve during life, the actual mechanism of valve function may be deduced to be as follows:

During diastole, the left atrial blood, due to the increase of the left atrial pressure, displaces the free margin of the valve sleeve into the ventricle ahead of its flow. At the level of the "annulus" at this time the valve is roughly circular, since the subaortic curtain also is displaced into the left ventricular outflow tract by the left atrial pressure. From palpation during life, it seems certain that during normal function of the heart, when the circulation is not at full capacity, the mitral valve does not open to the widest extent possible.

On systole, the high left ventricular pressure forces the valve tissue backward into the center of the valve orifice at the level of the "annulus" so that the "sleeve" falls in from all directions. At the same time, however, the subaortic curtain is displaced away from the left ventricular outflow tract (and into the left atrium) by the intraventricular pressure and, in this fashion, encroaches upon the circular shape of the mitral orifice at the level of valve attachment. Because of the difference in the lengths of the septal and mural portions of the valve sleeve, the line of valve closure is arcuate in shape. The relatively redundant free edge

of the valve at this time becomes "tucked" into many minute folds and irregularities to accommodate itself to the much shortened line of marginal contact (See Fig. 5B). This adjustment of the normally long, delicate valve edge to the much shorter line of contact which exists during systole is extremely important because the stenotic process tends to perpetuate or "freeze" the valve in this position (Fig. 7 AB). The mechanism of valve closure thus visualized differs basically from earlier descriptions in which the closing of the valve was visualized as a quasi-straight linear movement of two leaflets toward one another (See Figs. 1 & 2).

Pathology

The most important effect of the rheumatic process upon the mitral valve is the severe inflammatory reaction which involves the free edge of the valve. The fibrosis which follows the healing process results in shortening as well as in thickening of the margin of the valve (Fig. 8 ABC). This prevents the effortless unfolding of the "pleated" valve sleeve into the cavity of the ventricle in the direction of the diastolic blood flow. Undoubtedly, considerable shortening of the free edge may occur before any obvious physiological obstruction results. However, as the inflammatory process continues or is repeated, not only does this shortening of the margin cause impedance to flow, but the valve edges also may become adherent across the line of "folding" at either or both extremities of the "line of closure." In this fashion, the cross-fused folded free edge of the valve become the pathologically recognizable "commissures." In some stenotic valves the opening becomes reduced by the "purse-stringing" of the free edge only. This accounts for the fact that not infrequently no commissural scar can be made out or

FIGURE 11: Autopsy specimen — mitral valve of M. M., a 30 year old white woman who had been benefitted by mitral commissurotomy three years previously. Gradual hardening of the edges of the sizeable valve fissure without significant refusion of the commissures sufficed to re-establish severe valvular obstruction (See Fig. 3). There was a minimal element of regurgitation because of inexact coaptation of the valve edges. Forcible separation of the lips of the rigid "fissure" is shown here.

recognized in cases of mitral stenosis. But even in those cases in which well formed commissures are present their linear division will not restore a free edge of normal length. The "purse-string" contraction of the thickened valve margin will have preceded the cross-fusion which produced the actual commissures (Fig. 9 A and B).

The pathological process also produces thickening and contraction of the valve sleeve in such a way that the "mural" portion and the "junctional areas" usually become totally fibrosed and rigid, being converted essentially into an arcuate carnified shelf to which no functional mobility can be restored by any surgical technique known to us. A variable amount of fibrosis, shortening, and cross-adherence takes place between contiguous chordae tendinae, the involvement including those on the same side of the stenotic valve orifice as well as apposing ones. Usually, in the more advanced stages of mitral stenosis, such as are found frequently in patients who seek surgical help, one or both of the papillary muscles will be found to be adherent directly to the free but "purse-stringed" valve margin either due to intrinsic shortening of the chordae or to the formation of a complex fusion mass derived from organization of fibrinous exudate accumulated both upon them and upon the free valve margin (Fig. 10).

Criticism of the Commissural Concept

On the basis of this more complete understanding of the anatomical and pathological aspects of the mitral valve it readily becomes apparent that mere division of the zone of cross-fusion along the commissural scar line cannot be expected to restore a normal mechanism of valve function. Even the most complete commissurotomy procedure, including careful division of any adherent subvalvular structures, will produce but a comparatively rigid valvular "fissure" in which the combined

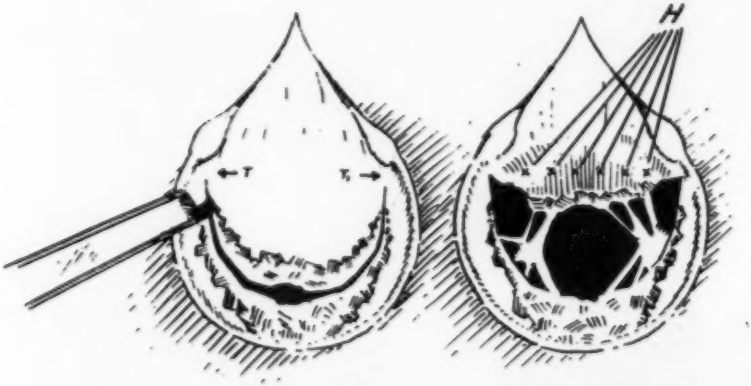

Figure 12A Valve Closed Figure 12B Valve Open

FIGURE 12—A and B: Diagrammatic representation of "Neostrophingic" mobilization for mitral stenosis: A tongue-like flap is created from the longer septal portion of the stenotic valve. It is essential that the lines of separation which begin in the commissural region be directed in smooth arcuate fashion toward the "target" points (T, and T_1), and that they are extended beyond the limits of scarring well into the "hinge" area (H).

lengths of both edges will be much shorter than the circumference of the free margin of the normal valve must have been (Figs. 9 B and 7 AB). Separation of the lips of the "fissure" cannot reduplicate the effortless unfolding of the delicately convoluted valve into the ventricle during diastole. At best, such a fissure can but widen appreciably during this phase of the cardiac cycle. Luckily, even any limited surgical enlargement of the stenotic orifice usually will improve the patient's clinical condition since the normal valve does not open to the fullest extent except upon maximal circulatory demand. As long as the opening is enlarged above a certain critical size, the symptoms will be relieved or, at least, considerably reduced. Unfortunately the existence of stiffened valve margins which cannot move apart widely, tends to permit gradual refusion of the divided commissures, as has been observed at autopsy as well as at reoperation[28] (Fig. 3). But even without such refusion, recurrence of the physiological effects of mitral obstruction may result from progressive hardening of the incompletely separated valve edges which will finally produce a fixed and rigid slit only (Fig. 11). The pressure of the blood within the left atrium can not rise sufficiently to widen such a slit to the extent necessary to achieve an effortless flow of blood across the mitral valve during diastole.

The New Concept
(Neostrophingic Mobilization of the Valve)

It probably is a truism to say that the aim of surgical treatment of mitral stenosis is the complete anatomical and physiological reconstruction of the mitral valve. However, since anatomical restoration to the status quo ante cannot be expected, as explained above, it would seem

FIGURE 13A: Lateral view demonstrating the proper line of division of the stenotic mitral valve in neostrophingic mobilization.

FIGURE 13B: Complete reconstitution of the stenotic valve. Note that the associated subvalvular fusion masses have been "split" extensively thus relieving the "subvalvular stenosis." Note also that the accomplished valve opening is of the same order of size as that of the natural valve passageway. Hinging upon the basal septal tissue provides a flap-valve or trap-door type of functional mechanism. Note the similarity to Fig. 14. Bailey et al, Courtesy of *Advances in Cardiology*, Editor: Prof. R. Hegglin. (S. Karger Ltd. Basle, Switzerland, 1959).

TABLE 1 — SUBJECTIVE IMPROVEMENT AFTER MITRAL COMMISSUROTOMY: STATUS OF SURVIVORS

Source	No. of Clinics	No. of Patients	Length of Followup	Marked Per cent	Moderate Good Per cent	Improved Per cent	Unchanged Per cent	Poor or Worse Per cent
Likoff et al	1	200	5-8 yrs.	28	27	17	25	3
Otto et al	1	106	1-5 yrs.	56	21	20	3	
ACCP*	34	5482	6 mos. plus	74.5		19.1		6.4
ACCP*	10	342	5 yrs. plus	70.2		25.5		4.3

*American College of Chest Physicians

acceptable if, by altering the anatomy of the valve suitably, we could provide conditions essential for normalization of the physiological derangements.

It has been found possible in surgical practice to create an anatomical "septal" leaflet by extending in arcuate fashion the division of both commissures (or the corresponding sites in the merely "purse-stringed" valve) into the valve substance well beyond the limits of normal chordal support. This division follows a semicircular line, the extremities of which are directed toward "target" points located just outside the trigonal terminations of the horseshoe shaped "annulus fibrosus." (Fig. 12 AB).

By deliberate and judicious surgical manipulations (based upon carefully acquired experience) this can be done without producing any

FIGURE 14: Mitral valve of terrapin heart. In this species there is no mural valvular tissue. Valve function and competence is provided by impingement of a freely swinging but chordally supported sail-like "septal leaflet" against a fleshy ridge which projects from the atrioventricular junction. Bailey et al. Courtesy of *Am. J. Card.*, Jan. 93, 1958.

TABLE 2 — ARTERIAL EMBOLIZATION FOLLOWING MITRAL COMMISSUROTOMY
(Left-sided Technique)

	Bailey Clinic (811 Patients)* per cent		American College of Chest Physicians (19 Clinics, 4463 Patients) per cent	
Cerebral		4.1		3.5
Nonfatal	1.9		1.9	
Fatal	2.2		1.6	
Peripheral		2.7		1.8
Nonfatal	1.5		0.6	
Fatal	1.2		1.2	
Total		6.8		5.3

*_Surgery of the Heart_, Charles P. Bailey, Philadelphia, Lea & Febiger, 19555.

physiologically significant regurgitation. Provided that cross-fused subvalvular structures are separated extensively, the resultant tongue-like "septal leaflet" becomes hinged freely upon its flexible basal tissue. It, then, can move in effortless fashion ahead of the blood flow into the ventricular cavity during diastole and will return during systole to abut against the arcuate, fibrosed, immobile shelf into which the "mural" and "junctional" portions of the valve have been converted by the pathological process (Fig. 13 AB). Although it is a readily demonstrable practical fact that extension of the valvular division beyond the limits or normal chordal support in this manner does not result in a physiologically significant degree of regurgitation (if any), provided the surgeon proceeds deliberately and carefully, the theoretical explanation for it is not so obvious. It has been suggested that the "coaptive" movement of the mobilized "septal" leaflet toward the fixed "mural" shelf due to the systolic pressure within the left ventricular outflow tract counteracts the "disruptive" force which is directed upward from the main cavity of the ventricle. Another explanation offered is that the newly established mechanism of valve function is similar to that observed in the terrapin in which the "mural" portion of valve is rudimentary and valve action is supplied by a "sail-like" movement of the "septal" leaflet (Fig. 14). Whatever the explanation, it is feasible in actual practice for the experienced surgeon in a high proportion of cases of mitral stenosis to fashion a new and highly efficient type of valve mechanism by the surgical technique described.

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Silent Myocardial Infarction

EKG Survey of Mentally Ill Patients at the Hudson River State Hospital

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Since 1925, numerous articles have been written,[1-8] about the electrocardiographic findings among mentally ill patients.** Many factors responsible for changes in these findings were mentioned: emotional disorders, endocrine dyscrasias, hyperventilation, dehydration and avitaminosis, tobacco, change of body position, vago-sympathetic imbalance, anxiety, respiratory movements, etc. Some of the authors[4] even mentioned: "Our electrocardiographic criteria may need radical revision," barring, of course, myocardial infarction. In the Chest Clinic of the Hudson River State Hospital we have about 3,000 electrocardiograms which were taken prior to 1959. There has never been a feeling that these contained any electrocardiographic changes which differ from the general population.

There have also been articles written about the occurrences of painless myocardial infarction in mentally ill patients,[9-10] with percentages varying from less than 1 per cent to as high as 38 per cent, but again in our routine examination we have not found such a high incidence, our findings being insignificant.

To ascertain the presence of electrocardiographic changes in mentally ill patients, and also to find out how many had myocardial infarction without noticeable symptoms or complaints, an electrocardiographic survey was undertaken. Fifteen hundred patients have been studied, they were selected because they had no sign or symptom of any cardiac condition as far as the physicians in charge of their care were concerned, after at least five years of hospitalization.

Some time ago the medical staff of the Hudson River State Hospital was put on the alert to watch for patients whose behavior changed suddenly, especially those who became unusually quiet, withdrawn from the other patients or showed any tendency to remain for long periods in bed with the covers drawn up over their heads. This behavior was first noted among known tuberculosis patients and through experience we have found that such behavior often indicates either reactivation or worsening of the pulmonary tuberculosis. The same change in behavior has been noted to apply to some serious cardiac diseases. These patients were excluded from our survey.

Electrocardiograms were taken by nurses trained as EKG technicians, and to avoid human error as much as possible, the tracings were read by three physicians: Dr. Jay R. Lockwood, Senior Attending in Medicine at Vassar Brothers Hospital, Poughkeepsie, New York, Dr. Robert I. Som-

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**Over 45 articles have been reviewed, but due to a limited space, only a few will be mentioned in "references."

mer, Senior Attending in Medicine at St. Francis Hospital, Poughkeepsie, New York, and the writer.

It is rather difficult to interpret the EKG's of mentally ill patients inasmuch as emotional factors come into play. It is a well known fact that the result of emotional stimuli to the cardiovascular system may be classified as follows: 1. "those involving cardiac rate and rhythm" (such as sinus tachycardia or bradycardia; of course when a very rapid rate is present for a long time, especially in the older group, there are temporary signs of myocardial ischemia present). 2. "those involving the vessels to localized areas, such as the skin, brain, heart or kidney" (dilatation or vasoconstriction which manifests itself by blushing, pallor, urticaria with vascular headaches, which in turn produces a rather different voltage in the EKG). 3. "those involving the circulation as a whole." (Such as a decreased peripheral resistance, visceral vasoconstriction and discharge of epinephrine from the adrenal glands. Increase of blood pressure and increase of peripheral resistance produce decreased cardiac output. It is well known that mental stress may exacerbate hypertension and its symptoms, so that the EKG also will be somewhat affected). 4. "those affecting the physical characteristics of the blood," (We found these changes to be irrelevant in our studies).

At times there has been difficulty in interpreting the so-called functional EKG abnormalities which have been reported[13] in young people free of cardiac disease when ST changes have been observed with marked depression of the segments in extremities and chest leads.

There are numerous articles about the high ST takeoff in normal patients and it has been stressed again that such findings are really to be kept in mind when interpreting a large number of EKGs, especially in mentally ill patients. There are also reports about the T inversion in healthy people with hyperventilation.

In our group, many patients, in addition to mental illness, also have glandular disfunction and at times it is trying to interpret the importance of the low voltage of QRST. In the absence of good reliable past history in our patients, the iso-electric ST is at times puzzling—double infarction might be manifested by such findings, but the age of such patients and their robust, healthy appearance speaks against such pathology. Often retakes clear up the puzzle.

First, it is interesting to note that there is some disagreement between the three physicians mentioned concerning the interpretations of the electrocardiographs. To eliminate as much discrepancy as possible, the three of us had separate readings and then the controversial tracings were re-evaluated in group meetings. Although we agreed in advance that certain "Standard Patterns" of myocardial infarction would be our guide, as well as other pathology (L. ventricular preponderance, coronary insufficiency, eschemia, etc.), numerous retakes were done to avoid wrong interpretations. Then we re-read all the abnormals, argued, and in the end came to final agreement.

The death rate has also been reviewed from 1952-1956 from the annual report which was published by the hospital. From a total of 2,014 patients, 1,477 died from cardiovascular disease. Unfortunately, only 170 could be autopsied and the following report is submitted:

	No. of Cases	Aver. Age	Aver. Yrs. Hospitalized
Arteriosclerotic Heart Disease (cardiac)	73	73	5½
Cerebral Hemorrhage	5	74	19
Coronary Occlusion	14	69	9
Acute Coronary Thrombosis	13	73	10
Rheumatic Heart Disease	1	63	7
Tuberculosis (2 miliary)	8	72	19
Carcinoma	25	65	18
Other Causes	31	48½	13½

Discrepancy between the number of deaths and the number of autopsies reported is because the New York State law requires permission from the legal next of kin to perform a post-mortem examination and many were refused.

Acute, sudden coronary thrombosis with infarction occurred in only 13 cases and the average age of deceased was 73 years. There were 14 cases of coronary occlusion, all sudden, with an average age of 69 years. From the combined group, totalling 27 cases, it was found that 75 per cent had cardiac pathology (generalized arteriosclerosis) upon admission, or after prolonged hospitalization, and the other 25 per cent fell in the age group where some arteriosclerotic heart disease findings would be expected. In other words, the autopsy reports did not reveal the presence of demonstrable myocardial degeneration, though one would expect such findings.

From this total 170 post-mortem examinations, only brief abstracts were available for study, and these were not too exact in regard to location and degree of the infarction. The slides which usually should accompany the abstract also could not be found, probably due to the system of filing, as the death cases are usually put in storage. The pathologist who performed the autopsies has been retired and we could not get information from him.

From the 1,500 EKG's taken, 203 showed abnormalities and only 25 could be called silent myocardial infarctions, since the EKG changes were definite. However, the rest of the pathological group will be studied in the future with serial EKG tracings. A complete review of the records of 25 patients shows that at no time did they have symptoms or complaints pertaining to cardiac pathology, although one would suspect some symptoms in the 59 with coronary insufficiency under normal circumstances.

The vast majority of EKG's (1,297) were normal, after minor controversies were ironed out by the reviewing group, and a review of the hospital records on these patients did not reveal anything unusual either in their physical examination by the ward physician or in their behavior. In private practice a great deal of thought and study has been directed toward determining the role of emotional factors in contributing to possible coronary disease or symptoms, and a great many articles have been written about this condition, especially in the differential diagnosis of true angina pectoris.[13-17] It is remarkable that severely psychotic patients are often felt to be so immersed in their own delusions and emotional problems that they give no hint of symptoms pertaining to cardiac disorders, even including angina. Their mental condition is such that we cannot get good histories from them. They do not call the atten-

tion of nurses or doctors to themselves and it is believed that many of them have lost "the meaning of pain." We cannot use many of the drugs which have been advocated as a test, nor can we use "Master's Test" or other helpful means because the majority are rather uncooperative, or even if willing, they become confused and bewildered, thus giving poor results as far as the tests are concerned.

However, since a new hospital policy of "open door" has been instituted a remarkable change in psychotic patients has taken place—they are more contented, appear happier and less secluded, and perhaps more cooperative, but still few could really cooperate to the full extent for our studies.

Searching for a simple test which could be easily performed, we were impressed by the EKG tracings of psychiatric patients who had been on rather large and prolonged dosages of thorazine. The tracings in the majority of these cases were with perfect isoelectric lines, clear and free of doubtful variations of the P, Q, RST, and with a slow pulse rate. Furthermore, in the majority of the thorazine group the EKGs were normal, except for a few bradycardias, which were found in spite of the fact that tachycardia had previously been reported.

Assuming that the medication might be helpful in the differential diagnosis of coronary insufficiency, we used, as a test, thorazine 100 mg. tablets three times a day for three days, and then repeated the electrocardiograms. Fourteen patients were selected whose original EKG's were in the group of doubtful tracings, but judged by the consensus of opinion of the three participating doctors, were within normal limits.

We did not include in this group anyone who had an elevation of blood pressure, (except No. 3 — 180/108 — 45 years of age), and the average age was 45 years. (Two were under 20, three over 60, and the rest were scattered between the ages of 25 and 59). The results of the electrocardiograms were rather unexpected:

1. Nine cases showed no change.
2. Four showed some changes but these were not significant enough to warrant evaluating the tracing differently.
   (a) No. 9-T waves became lower in precordial leads, rate increased from 62 to 82. P2 became of much less voltage.
   (b) No. 11 — QRS in AVL became of higher voltage and T became negative.
   (c) No. 12 — Pulse slowed down from 138 to 90. ST less depressed in V4, V5 and V6.
   (d) No. 13 — T negativity in V4, V5, and V6 less pronounced.
3. One case (No. 5) after thorazine EKG showed signs of posterior wall infarction which was without the usual symptoms and was unquestionably silent, perhaps caused by the thorazine medication. On the other hand, if medication could produce a severe or even moderate hypotensive action, then we should really have much more frequent infarctions since a great number of our patients receive such drug. In fact, from normal EKG patients, 331 were on drug, 966 without it; from 203 abnormal on drug, 42 remaining; 161 no drug. On the other hand, from 59 Coronary Insufficiency cases — 13 have been on thorazine.

RESUME

From 1500 cases studied	849 men (56.6 per cent)	651 women (43.4 per cent)
Total cases abnormal 203	125 men (61.57 per cent)	78 women (38.43 per cent)
Average age of abnormal 64.425 yrs.	64.13 yrs. men	64.88 yrs. women
Average yrs. hosp. of abnormal 20.618 yrs.	21.274 yrs. men	19.602 yrs. women

Blood pressure of abnormal	High Per cent	Norm. Per cent	Low Per cent	Unknown
Men —	31 (25)	76 (61.2)	17 (13.7)	1
Women —	27 (35)	46 (59.7)	4 (5.1)	1
Total	58 (28.8)	122 (60.6)	21 (10.4)	2

	Abnormal Cases	Percentage	On Tranquillizers
Infarct (incl. 3 ques.)	25	0.016 or 1.6	8
Rt. BBB	18	0.012 or 1.2	3
Lt. BBB	12	0.008 or .8	2
Coronary Insufficiency	59	0.038 or 3.8	13
Left vent. prepond.	28	0.017 or 1.7	5
Non-specific	3	0.002 or .2	0
Myocardial ischemia	1	0.0006 or .06	0
Auricular Fibrillation	4	0.0026 or .26	2
Rt. vent. hyper.	3	0.002 or .2	0
Rheumatic heart	2	0.0013 or .13	2
Paroxysmal supraventric tachy	1	0.0006 or .06	1
AV Block	33	0.022 or 2.2	5
Left vent. strain	12	0.008 or .8	1
Congenital defect	1	0.0006 or .06	0
Mult. vent. extra-systoles	1	0.0006 or .06	0
Total Abnormal Cases	203	0.135 or 13.5	42

BREAKDOWN OF ABNORMAL BY MENTAL DIAGNOSIS

Diagnosis		Abnormal	Percentage	Number in Hosp.
Psychosis with Mental Deficiency		9	.044 or 4.4	219
Alcoholic Psychosis		17	.082 or 8.2	293
Psychoses due to other Metabolic Diseases Assoc. with Organic Changes		1	.004 or .4	42
Paranoid with Paranoid Condition		1	.004 or .4	107
Involutional Psychosis		12	.059 or 5.9	283
Cerebral Arteriosclerosis		12	.059 or 5.9	547
Senile Psychosis		7	.034 or 3.4	390
Psychosis due to Trauma		4	.019 or 1.9	44
Psychosis-Psychopathic Personality		2	.009 or .9	59
Psychosis-Epidemis Encephalitis		1	.004 or .4	11
Psychoneurosis		4	.019 or 1.9	124
Manic Depressive	—Total	5	.024 or 2.4	249
	Mixed	2	.009 or .9	
	Paranoid	1	.004 or .4	
	Manic	1	.004 or .4	
	Simple	1	.004 or .4	
Schizophrenia	—Total	110	.541 or 54.1	2,942
	Hebephrenic	26	.128 or 12.8	
	Catatonic	7	.034 or 3.4	
*(Note on lobotomy group below)	Paranoid	62	.305 or 30.5	
	Mixed	6	.029 or 2.9	
	Simple	10	.048 or 4.8	
Psychosis — Cerebral Syphilis		3	.014 or 1.4	29
General Paresis		7	.034 or 3.4	190
Epilepsy		1	.004 or .4	107
Undiagnosed Psychosis		1	.004 or .4	2

*From 46 post-lobotomy group studied — only one abnormal found. This was a Rt. BBB, included in with Schizophrenia totals.

*From a total of 90 morons, idiots, and imbeciles at Wassaic State School, 30 were able to be studied. In this group there was no abnormality.

*Totals in the extreme right column, under number in hosp., are based on the 1958 total census of 5,713. Of this number, there were 2,507 men, 3,206 women.

However, the previous warning that hypotensive effect might be produced by certain tranquilizing drugs and that it should not be used in either generalized arteriosclerosis or cardiovascular disease, still stands. Thorazine was abandoned as a test.

One and one half years later, 64 cases were retaken by mistake and in eight cases the EKG's were different from previous ones:

(1) No. 36 — the first was called normal, 2nd plus 1st, AV block.
(2) No. 146 — first was normal; 2nd — AV block.
(3) No. 156 — first normal; 2nd — posterior wall infarction.
(4) No. 193 — first normal; 2nd — left ventricular strain.
(5) No. 176 — first normal; 2nd — intraventricular convection disturbance.
(6) No. 201 — first normal; 2nd — ischemia due to tachycardia.
(7) No. 292 — first ischemia; 2nd — normal.
(8) No. 946 — first mycardial insufficiency; 2nd — normal.

These 64 cases bring up a very interesting question as to how to conduct a survey, how many patients should be studied and whether it is necessary to follow up the normals, and if so, for how long and at what intervals. Going through 1500 cases we found the following percentages:

From 62 — there were 0.6 per cent infarctions found.
From 100 — 1 per cent
200 — 2.5 per cent
300 — 3 per cent
400 — 1.5 per cent
800 — 1.6 per cent
1000 — 1.7 per cent
1200 — 0.7 per cent
1500 — 1.6 per cent

Judging from these figures, perhaps 800 would be sufficient for study of total hospital population — over 5000. As far as a follow-up is concerned, no definite rule can be advocated.

Beginning June 15, 1959, we hope routine electrocardiograms will be taken on admission of those patients over 40 years of age, and in the younger group also if there is any history of pre-existing cardiac disease. Thus, we shall have comparison material for future studies. We also plan to do EKG's on all patients following completion of electric shock therapy, in addition to the routine tracing which has always been taken prior to the electric shock treatments as well as all patients prior to surgery.

The "silent myocardial infarction" will require study and research in every institution housing a great number of inmates; results should be useful and interesting. Incidentally, included in our normal group were 30 cases of imbeciles and morons and we have come to the conclusion that in order to keep the coronary vessels in a healthy condition, one should perhaps be more idiotic and moronic.

SUMMARY

1. Silent myocardial infarction occurs among mentally ill patients but in our study the percentage is rather low (1.6 per cent) as compared with previous reports.

2. There is no relationship between infarction and any given psychiatric diagnosis: Infarction is not more prevalent in one psychiatric group than another.

3. Cardiac pathology, other than myocardial infarction, (13.5 per cent) exists in comparitively greater number but the majority of these diagnoses could be made only with the help of EKG.

4. Wards designated for cardiac patients should be investigated with EKG as well as wards housing diabetics.

5. It seems desirable that EKG studies be made on admission of patients over 40 years of age, on pre-surgery cases, pre and post ETC and all cases which might be suspicious for presence of cardial disease.

6. If from 1500 cases studied, 203 new cardiac cases were found, it is safe to assume that another 743 cases could be cardiacs, but most likely free of symptoms or complaints or perhaps some are already on cardiac wards.

ACKNOWLEDGMENT: The writer is grateful to all the persons who participated in this study. To Dr. Robert C. Hunt, Director of the Hudson River State Hospital, who made it possible to continue this work which was undertaken while Dr. O. A. Kilpatrick was Director. Practically every member of the Staff, nurses, and other employees, helped in gathering data, particularly the Staff in the Tuberculosis Department who took the Electrocardiograms and tabulated many data.

RESUMEN

1. Se pueden presentar infartos silenciosos del miocardio en los enfermos mentales pero según nuestro estudio, el porcentaje es más bien bajo (1.6 por ciento comparado con otras comunicaciones).

2. No hay relación entre el infarto y cualquier diagnóstico psiquiátrico; el infarto no es más frecuente en uno u otro grupo.

3. La patalogía cardiaca además del infarto cardiaco (13.5 por ciento) existe en número comparativamente mayor, pero la mayoría de estos diagnósticos pudo hacerse sólo mediante el E.C.G.

4. Los servicios para enfermos cardiacos deben ser investigados por el electrocardiograma de la misma manera que lo son para la diabetes.

5. Es de desearse que se hagan estudios electrocardiográficos de ingreso en los enfermos mayores de 40 años y en todos los casos sospechosos de enfermedad cardiaca.

6. Si en 1,500 casos estudiados, 203 nuevos cardiacos se han encontrado, es de presumirse que otros 743 casos podrían ser cardiacos pero muy probablemente sin síntomas o tal vez algunos ya están en los servicios de cardiacos.

RESUMÉ

1. L'infarctus myocardique silencieux survient chez des malades mentaux, mais dans notre étude, le pourcentage est plutôt faible (1,6% selon la comparaison avec des rapports antérieurs).

2. Il n'y a pas de rapport entre l'infarctus et un diagnostic psychiatrique donné: l'infarctus n'est pas plus prédominant dans un groupe psychiatrique que dans un autre.

3. La pathologie cardiaque, autre que l'infarctus myocardiaque (13,5%) existe dans un nombre de cas comparativement plus grand, mais la majorité de ces diagnostics ne pourraient être faits qu'avec l'aide de l'électrocardiogramme.

4. La menace d'une cardiopathie devrait inciter à faire un électrocardiogramme exactement comme l'on fait quand on s'occupe de diabétiques.

5. Il semble désirable que les études électrocardiographiques soient faites à l'admission des malades âgés de 40 ans et plus, pour les cas pré-chirurgicaux et pour tous ceux qui pourraient être suspects d'atteinte cardiaque.

6. Si sur 1.500 cas étudiés, 203 nouveaux cas cardiaques ont été trouvés, il est raisonnable de penser que 743 autres pourraient être cardiaques, mais qu'ils sont vraisemblablement indemnes de symptômes ou de douleurs, ou peut-être que quelques-uns et sont déjà au stade des menaces cardiaques.

ZUSAMMENFASSUNG

1. Stumme Myokardinfarkte kommen bei Geisteskranken vor, jedoch nach unserer Untersuchung in ziemlich geringer Zahl (1,6% im Vergleich zu früheren Berichten).

2. Es besteht keine Beziehung zwischen Infarktgenese und der gegebenen psychiatrischen Diagnose: Infarkte kommen in keiner bestimmten Gruppe von psychiatrischen Patienten häufiger vor als in einer anderen.

3. Pathologische kardiale Befunde, vom Myokardinfarkt abgesehen, (13,5%) kommen in vergleichsweise gröserer Häufigkeit vor, aber die grössere Zahl dieser Diagnose konnte nur mit Hilfe des EKG gestellt werden.

4. Für Herzkranke bestimmte Krankenstationen müssen mit EKG untersucht werden, ebenso wie Abteilungen, auf denen sich Diabetiker befinden.

5. Es dürfte sich empfehlen, EKG-Untersuchungen vorzunehmen, wenn Patienten von mehr als 40 Jahren aufgenommen werden, wenn operative Eingriffe vorgesehen sind, vor und nach ETC, und bei allen Fällen, bei denen der Verdacht besteht auf das Vorliegen von Herzkrankheiten.

6. Wenn unter 1500 untersuchten Fällen 203 neue Herzfälle entdeckt wurden, so kann man sicher annehmen, dass noach weitere 743 Herzkranke darunter sind, jedoch höchstwahrscheinlich ohne Symptome oder Beschwerden; vielleicht befinden sich aber auch einige schon auf einer Herzstation.

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SUMMARY OF CURRENT THERAPY

Management of Paroxysmal Tachycardia

Paroxysmal tachycardias frequently occur in healthy individuals and are characterized in many instances by their short duration and paucity of symptoms. This explains why they are only occasionally seen by medical students and can seldom be demonstrated in lectures or bedside rounds. Therefore, many physicians are faced with a paroxysmal tachycardia for the first time when already in practice and this may be one of the reasons why this diagnosis is so often missed. Another reason accounting for the failure to diagnose a paroxysmal tachycardia is that the heart rate need not be very rapid. Any pacemaker forming impulses more rapidly than the basic rhythm will take over. Accordingly, paroxysmal tachycardias with rates of 130 or less may be observed. Such a state often is diagnosed as a sinus tachycardia.

The correct diagnosis of a paroxysmal tachycardia is most important in a patient with acute myocardial infarction. The increased rate may be accompanied by a fall of blood pressure, liver enlargement and other signs of congestive failure or shock which erroneously may be thought to be due to the primary lesion. In such patients the entire clinical picture may improve if the tachycardia is arrested by carotid pressure.

Even when the tachycardia produces symptoms the recognition may be difficult as the patient may not see his physician at the time when the tachycardia is present and the symptoms may not be associated with a tachycardia. These patients may complain only of anginal pain at rest (due to tachycardia associated with coronary sclerosis), right upper abdominal pain (due to acute congestion of the liver), fullness of the neck (due to congestion of the neck veins). Palpitations often are absent.

Many physicians have undue concern about paroxysmal tachycardias when they find a patient with a heart racing more than 200 times per minute and they try to abolish this abnormality with means which endanger the patient much more that does the tachycardia. Actually in most cases the attacks are harmless. In one of our observations a patient with a rheumatic mitral stenosis could walk up a low hill to a hospital in spite of atrial flutter with a ventricular response of 328 beats per minute.

Certain of paroxysmal tachycardias are to be treated as emergencies. These include attacks complicating myocardial infarctions and those occurring in patients who are on the verge of decompensation.

Since, in the absence of such emergencies, a tachycardia with a ventricular rate of about 200 may be tolerated for many days without serious consequences, one should not attempt to treat a tachycardia without first taking an electrocardiogram. The treatment as well as the prognosis will depend on the type of tachycardia found.

Atrial flutter responds less rapidly to therapy than paroxysmal atrial tachycardia. The treatment of flutter should be done under hospital supervision. Ventricular tachycardia is even more ominous and requires immediate hospitalization.

The electrocardiogram may clarify many iatrogenic tachycardias (digitalis toxicity) which otherwise would go unrecognized or would be aggravated by continued therapy.

Except in the special emergencies mentioned above a tachycardia should not be treated by an intravenous injection of the numerous drugs recommended for this purpose. It cannot be denied that an intravenous injection of quinidine or quinine, magnesium sulfate or some of the pressor amines brings often an instantaneous success. However, all these injections may cause very serious effects and, in a small percentage of patients, even death. Such a risk is not justified in an attack which can be terminated by other means. Even a normal heart will be dilated and the systole weakened after an intravenous injection of quinidine. The frequency of such accidents is greater in a damaged heart and diastolic standstill may be observed. Many of the substances which quickly abolish an attack of tachycardia also may precipitate one. In a recent publication the use of levophed was advocated for paroxysmal tachycardias but at the same time it was recommended that procaine amide be available for the development of ventricular tachycardia. This recalls the advice to have atropine ready for the treatment of accidents which developed when mecholyl was used for an atrial tachycardia. As with the other drugs mentioned, calcium chloride and prostigmine have led to fatal accidents when administered intravenously for the treatment of a paroxysmal tachycardia. As an example of the folly of therapeutic conjecture a physician gave epinephrine to a patient with paroxysmal tachycardia. The patient became pulseless and was unconscious for several minutes. On recovery the tachycardia had stopped. The conclusion from this one observation was that epinephrine should be used for the therapy of paroxysmal tachycardia!

Recent studies, particularly by Corday and his colleagues have shown that the pressor amines such as levophed, aramine, isuprel or vasoxyl are of great value for the treatment of ectopic rhythms in acute myocardial infarctions accompanied by shock or with shock threatening.

When an injection is needed to terminate a paroxysmal tachycardia as rapidly as possible the drug of choice is digitalis. There is only one contraindication to intravenous digitalis administration; the patient may be already under the influence of the drug. If no digitalis had been received for 3 weeks prior to the examination, digitalis will not be harmful. It often helps and should be given even in ventricular tachycardias. We have observed it abolish even a ventricular tachycardia with alternating form of ventricular complexes. The peak of action of the drug, provided a pure glycoside is given, occurs within 60 minutes. It is of interest to note that while carotid pressure is often ineffectual in abolishing paroxysmal atrial tachycardias prior to digitalis administration, the same pressure about one hour after the injection will often produce reversal to normal rhythm.

In ventricular tachycardias the injection of pronestyl may be life saving. If given intravenously the injection must be very slow and the blood pressure constantly under control. Bellet has recommended the intramuscular injections of 0.5 to 1.0 gram of pronestyl gluconate which de-

serves wider use since it apparently does not provoke a dangerous hypotension.

Although statistics vary on the efficacy of vagal reflexes in abolishing a paroxysmal atrial tachycardia the frequency of success and the absence of harmful side effects certainly justifies their use first. Carotid pressure is the most effective form of vagal reflex and should be tried carefully. Some attacks respond immediately to a mere touch in the region of the carotid sinus while in others the sensitive spot may be found after several attempts and strong pressure must be exerted to elicit an effect. We do not advocate the use of "carotid massage;" the effect on the heart will be the same as with pressure but massage implies compression of the carotid artery for a longer period and this brings the danger of convulsions and even hemiplegia. This will occur in young healthy individuals with an imperfectly functioning circle of Willis and will be more common in the elderly where one of the internal carotid arteries is so often narrowed or occluded. Carotid pressure, exerted for just a few seconds is harmless even in these patients.

Although many statements in the literature stress the lack of response of ventricular paroxysmal tachycardias to carotid pressure this is not always the case. Wenckebach and Winterberg described in their book on cardiac arrhythmias a patient which the present writer had the opportunity to study repeatedly, in whom carotid pressure would immediately abolish a definite ventricular tachycardia.

Other methods of producing vagal reflexes include forced rapid inspiration, the Valsalva experiment, pressure exerted on the upper abdomen, gagging, or bending forward. It reflects badly on the responsible physician if a patient knows better than he, how to terminate his attacks. An intelligent patient who, while having an attack strains at stool and finds that during this procedure repeatedly an attack terminates will do the same "Valsalva experiment" as soon as the next attack appears. Another patient, who develops during an attack an acute congestion of the liver with vomiting will soon learn that the attack ends with the vomiting and will at the onset of one of the next attacks provoke vomiting by putting his fingers into his throat. One of our patients found that she could terminate every attack by scrubbing the floor; unwittingly she elicited a vagal reflex by bending and squatting.

Most attacks which do not respond to one of the vagal reflexes will subside with a few oral doses of quinidine, if the drug cannot be given because of hypersensitivity or if the response is not satisfactory, oral digitalis therapy is the next choice. Since most investigators believe that paroxysmal tachycardias are due to rapid impulse formation in a cell, anything which changes the electrolyte pattern and transmembrane electrolyte flow in this cell may abolish a tachycardia. Therefore, an occasional success may be seen with rauwolfia, atarax or antihistamine preparations.

Prevention of new attacks is no problem if they occur rarely. No drug therapy will be advisable in such patient. In some rate patients one will be faced with a therapeutic problem such as when attacks of tachycardia of rather short duration are present almost constantly. These patients

with "extrasystoles à paroxysms tachycardiques" (Gallavardin) or repetitive tachycardia" of Parkinson and Papp often require very large doses of quinidine or digitalis for control and these may not be well tolerated. Such tachycardias may gradually subside often after years but in some instances slowly lead to cardiac dilatation, cardiac failure and death.

In other patients, the tachycardias recur often, several times each month or even weekly. The usual preventive doses of quinidine or digitalis are too small and ineffective and larger ones are not advisable because of unpleasant side effects. A combination of moderate doses of each drug is indicated in such patients. If ineffective often psychotherapy and encouragement is all that remains to tide patients over the critical period and are of inestimable value.

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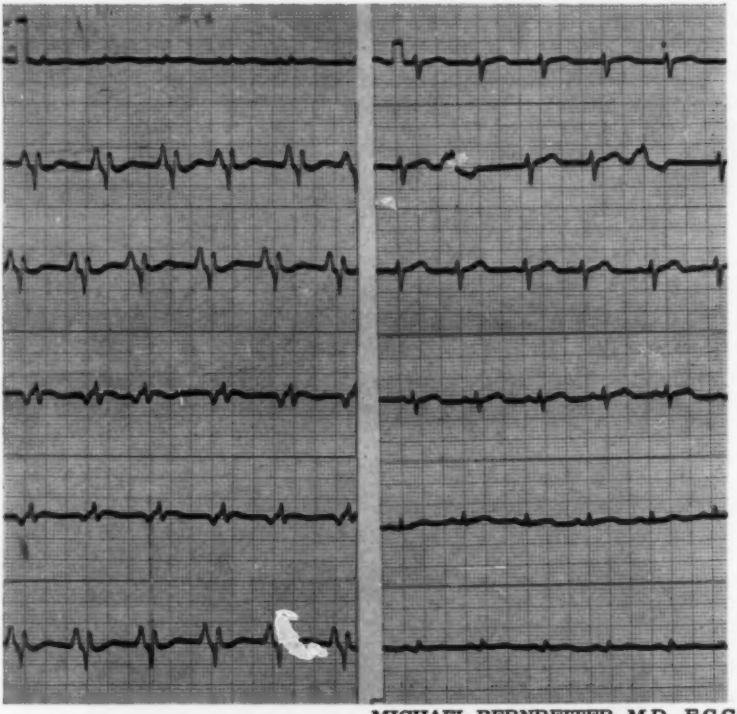
ELECTROCARDIOGRAM OF THE MONTH

Cor Pulmonale Simulating Posterior Myocardial Infarction

This electrocardiogram was obtained from a 60 year-old man who has had emphysema, asthma and chronic bronchitis for years. His blood pressure was 138/86 and his chest x-ray film showed a normal size heart and pulmonary emphysema. The P waves in Leads II, III and aVF are typical for P pulmonale, so characteristic for chronic cor pulmonale. The interesting feature of this tracing is the deep Q waves in Leads II, III and aVF, showing the well known pattern of posterior myocardial infarction. This patient never had heart trouble and serial electrocardiograms in the last five years never showed any significant changes.

These findings prove again how important it is to realize that severe cor pulmonale may give rather classical findings of posterior myocardial infarction. This man came to autopsy and there were no signs of an old or recent posterior wall infarction. The prominent Q waves in Leads II, III and aVF in such cases are explained by marked clockwise rotation of the heart around the longitudinal axis and posterior displacement of the apex.



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X-RAY FILM OF THE MONTH

Clinical Information

This 32 year old white girl entered the hospital in March, 1959 after having three episodes of hemoptysis in the week prior to admission. Her past history was noncontributory. On physical examination, she did not appear ill. Peculiar skin lesions were present in a "butterfly" distribution about her cheeks and nose. There were several nodular thickenings under the skin of the lumbar area. A skull roentgenogram showed faint intracranial calcification in the temporal area. Roentgenograms of the hands and feet showed wavy irregular periosteal thickening of the metatarsals and metacarpals.

Two weeks after admission, she had a sudden sharp right chest pain. A chest film revealed right pneumothorax. The lung gradually re-expanded during the next few weeks.

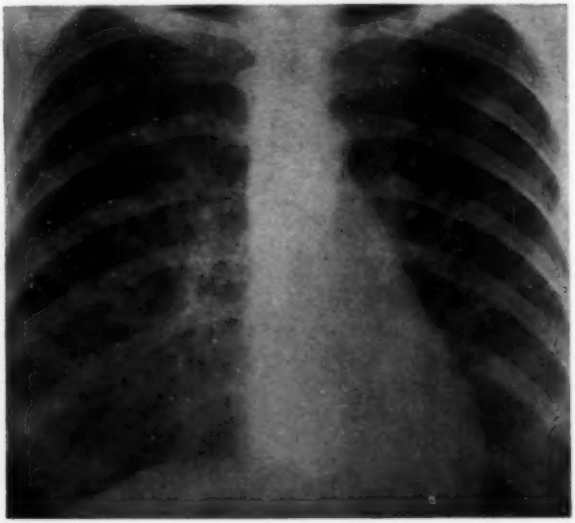
ANSWER

Tuberous Sclerosis

Syn.: epiloia, Bourneville's disease

In its full-blown form tuberous sclerosis consists of epilepsy, mental deficiency, cutaneous lesions, congenital defects, and tumors. The disease is probably one of disordered development beginning early in embryonic life, although a minority group feels that the malady is primarily neoplastic. The incidence is estimated as one in 150,000 in the general population.

Tuberous sclerosis actually gets its name from the potato-like nodules (tubera) occurring in the brain. Microscopically these lesions consist of massive glial scar tissue containing abnormally large glial and nerve cells of bizarre pattern. Classically, these nodules are located in the walls



of the lateral and third ventricles. Calcification of the nodules may occur, particularly in the region of the basal ganglia.

Adenoma sebaceum is the skin manifestation most widely associated with tuberous sclerosis. These skin lesions are distributed in a butterfly pattern over the nose, cheeks, and nasolabial folds, and consist of overgrown sebaceous glands embedded in hypertrophied connective tissue. Other skin lesions include subungual and periungual fibromas. Peau chagriné are raised white nodular areas under the skin found in the lumbo-sacral region. The retinal tumors of tuberous sclerosis, called phacomas, are whitish, lentil shaped, astrocytic tumors.

Renal tumors are described in 50 to 80 per cent of the cases. These tumors are usually small, sharply defined, cortical in location, and frequently bilateral. Occasionally, they may be quite large and are readily mistaken for hypernephromas. Histologically, they are hamartomas.

The bone changes are limited to the skull, hands, and feet. In the skull patchy zones of increased density are found on the roentgenogram. Cystic changes may be present in the phalanges of the hands and feet and there is sometimes a wavy irregular periostitis of the metatarsals and metacarpals.

Tumors of many other organs including rhabdomyomas of the heart have been associated with the disease. Congenital anomalies of all organ systems of the body have also been reported.

Pulmonary involvement in tuberous sclerosis is infrequent; there have been only about 20 cases reported in the literature. Most have occurred in women 20 to 40 years of age. Although the other stigmata of tuberous sclerosis, such as adenoma sebaceum, are present, mental deficiency has been infrequently associated with pulmonary involvement. Despite the widespread extent of the process in the lungs, cough has not been a salient feature. At autopsy multiple small cysts have been disclosed in a solid-appearing lung. Rupture of subpleural cysts accounts for the pneumothorax which occurs in one-third of the cases. Microscopically the cysts show no specific lining and the walls are made up of connective tissue containing numerous blood vessels. A consistent feature is the presence of smooth muscle with a cellular arrangement similar to that of myoma and the term *diffuse myomatosis* has been applied. The chest roentgenogram shows a "honeycomb" appearance, as in the present case, or a widespread coarse mottled miliary pattern.

ACKNOWLEDGMENT: Case presented by permission of Lee S. Rosenberg, M.D., The Jewish Hospital, Cincinnati, Ohio.

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Thoracic Surgery in the Presence of Pulmonary Insufficiency and Disability

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The advances accomplished during the past two decades in anesthesia, surgical technique, pre-and postoperative care and the understanding of pathologic physiology have rendered it possible to perform successful thoracotomies and lung resections on patients with low pulmonary function. The following cases will illustrate some of these points.

Case 1: A 32 year old woman had severe sacculocylindrical bronchiectasis of the right lower and middle lobes (Figs. 1 and 2). Removal of the diseased and contracted lobes did not alter significantly her low pulmonary function tests (Table I). The importance of clearing secretions and having the patient in optimal condition before the determination of these tests is stressed. The postoperative change in the arterial oxygen saturation, although slight and within the limits of error, may reflect the elimination of venous blood passing through the diseased lobes without being properly oxygenated. Measurement of partial pressures of oxygen may have shown greater changes.[1] The postoperative course was complicated by a severe transfusion reaction, bleeding, paralytic ileus and empyema. The immediate postoperative bleeding necessitated re-exploration and the empyema which occurred later responded to rib resection and open drainage. With a maximum breathing capacity of about 43 liters and a one second vital capacity of 28 per cent and careful postoperative tracheo-bronchial toilet she withstood well the surgical procedures and complications and was in good health when last seen in our clinic.

Case 2: A 53 year old man had his left lung removed because of extensive fibrocaseous tuberculosis. His preoperative maximum breathing capacity was only of 31 liters and about [illegible] per cent of his predicted value. Such a low value is always accompanied by a low [illegible]terial pressure of oxygen[1] and denotes pulmonary insufficiency bordering disability. The decrease in maximum breathing capacity is proportionately more than the decrease in vital capacity pointing towards an element of dysfunction of the obstructive type.[2] Despite such low pulmonary function, the left lung was removed. It was reasoned that its contribution to pulmonary function was extremely limited and probably detrimental. That proved to be so both subjectively and objectively (Table II).

Case 3: A 65 year old man suffered from bullous emphysema and had severe pulmonary disability manifested by his inability to walk more than a couple of steps at a time. His maximum breathing capacity was of 15 liters and his one second vital capacity of 29 per cent. Because of the presence of huge lung cysts particularly on the left (Fig. 3), a left postero-lateral thoracotomy was performed, two huge air cysts were excised and the visible bronchial openings closed. Parietal pleurectomy was done, the remainder of the lung being studded with subpleural blebs. The postoperative course was uneventful. The use of bronchodilators, tracheo-bronchial hygiene and antibiotics enabled us to successfully carry through a thoracotomy on a patient with such a severe degree of pulmonary disability. He did feel better for a while, before succumbing to his basic disease about a month later, cor pulmonale and heart failure being the dominant features.

Discussion

The postoperative pulmonary function depends on the balance between the ventilation, distribution, diffusion and perfusion factors in the resected and remaining lung tissues. Removal of a poorly ventilated and well perfused lung will improve function whereas removal of a poorly ventilated and poorly perfused lung may not alter it. Thus pulmonary insufficiency as estimated by a certain pulmonary function test may not be a contraindication to surgical extirpation of portions of lungs. Judgment along these lines may prevent or foretell the onset of pulmonary disability as a result of resectional therapy to a patient suffering from pulmonary insufficiency. Lung insufficiency and lung disability should be distinguished.[2] In the latter, the patient is unable to go on with his daily activities. The first two cases illustrate that extensive resections of diseased lung parenchyma may be performed without significantly altering the pulmonary function. Poorly ventilated and poorly perfused lung segments are eliminated, toxicity and secretions minimized. All three cases demonstrate that, at present, patients with extremely low pulmonary function can be carried safely through a thoracotomy.

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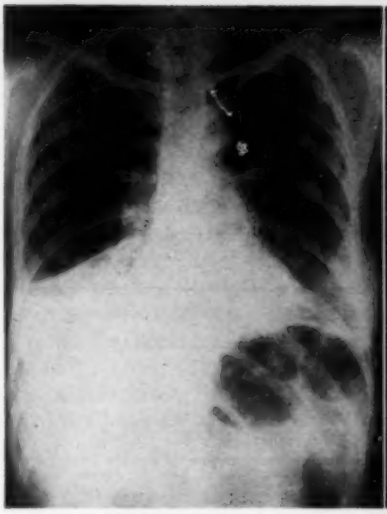

FIGURE 1

FIGURE 2

FIGURE 1: Preoperative postero-anterior x-ray film of the chest showing the contracted middle and right lower lobes. FIGURE 2: Preoperative bronchogram reveals the aerated portion of right lung was only the upper lobe. Note extent of disease in right lower and middle lobes.

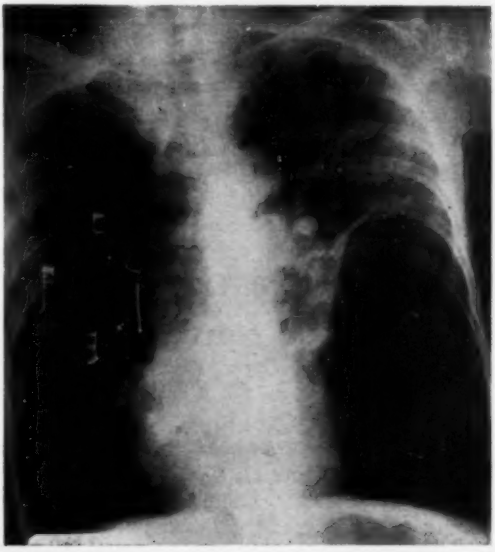

FIGURE 3 *(Case 3)*: Note the large air cysts, particularly on the left side.

TABLE I — PULMONARY FUNCTION TESTS PRE AND POST RIGHT LOWER AND MIDDLE LOBECTOMIES FOR SEVERE BRONCHIECTASIS

	MBC*	VC**	TVC***	Arterial Oxygen Saturation
Preoperative values				
Actual	42.7	1.27	28	93
Predicted	91.16	2.91		
Per cent of predicted	46.8	43.64		
Postoperative values (3 months)				
Actual	39.4	1.23	37	96
Predicted	91.16	2.91		
Per cent of predicted	43.22	42.26		

*Maximum breathing capacity in liters/minute.
**Vital capacity in liters.
***Timed vital capacity, 1 second per cent of VC.

TABLE II — PULMONARY FUNCTION TESTS PRECEDING AND FOLLOWING LEFT PNEUMONECTOMY FOR A DESTROYED LUNG

	MBC*	VC**
Preoperative values		
Actual	31	1.750
Predicted	97	3.570
Per cent of predicted	32	49
Postoperative values		
Actual	27.5	1.510
Predicted	92.2	3.500
Per cent of predicted	29.8	42.2

*Maximum breathing capacity in liters/minute.
**Vital capacity in liters.

TABLE III — BEDSIDE PULMONARY FUNCTION TESTS OF A PATIENT SUFFERING FROM SEVERE BULLOUS EMPHYSEMA

	MBC*	VC**	TVC***	Arterial Oxygen Saturation
Preoperative values				
Actual	15	1.1	29	91
Predicted	117.7	4.0		
Per cent of predicted	12.6	36.3		

*Maximum breathing capacity in liters.
**Vital capacity in liters.
***Timed vital capicity, 1 second per cent of VC.

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Air Travel in Cardiorespiratory Disease

Report of the Section on Aviation Medicine
Committee on Physiologic Therapy
American College of Chest Physicians

Passenger transport by air is rapidly expanding. Whereas passenger transport by rail has been shrinking, and by bus has been remaining about constant, the number of passenger miles logged on scheduled airlines all over the world is rapidly rising year by year. In fact, this is rising at such a rate that the necessary equipment ordered by airlines to meet their present needs cannot always be fulfilled by the manufacturers. Also, the necessary public works such as airports, maintenance hangers and so forth, have been lagging far behind the needs of the air transport industry. To this must be added the increasing number of private planes and the widespread use of chartered and non-scheduled flights. The reasons for the rise of aircraft travel are many, the most obvious of which are:

1. Speed
2. Cleanliness
3. High standard of comfort
4. Relative inexpensiveness,

compared to any other form of transport at equivalent comfort and convenience.

However, although these advantages for normal people are obvious, yet there is some hesitancy in encouraging air travel with people who are suffering from a number of disease processes. Of these groups, one of the most important is patients with cardio-respiratory disease. In these patients, altitude exposure is considered to be the major problem although other factors, such as psychological factors, noise and other similar characteristics of air travel are important. It must be remembered that the mortality from cardio-respiratory disease per passenger mile traveled by air is far below that of rail or bus transport at the present time.

The following table shows a list of those aircraft in common use and projected use within the next year in the United States in particular, but also throughout the rest of the world.

From this table, one can see that exposures above 5,000 feet in altitude are common place in pressurized aircraft and that in the jet transports these may at times be somewhat higher. These have been calculated on the basis that the maximum pound per square inch differential pressure between the outside and cabin pressure will be reached and will be maintained at the operating level. This may not be true under normal airline operation conditions in particular circumstances and moreover, in order to avoid for example, stormy weather, planes may exceed their usual operation altitude. This is shown well in the Douglas DC-7 where a member of this committee has logged 32,000 feet external altitude for a period of over one hour. The reverse is equally true in that aircraft may fly much lower over certain routes than their normal cruising altitudes.

Company & Aircraft	Δ psi	Operating Altitude	Cabin Altitude	Comments
Boeing Airplane Co. Seattle, Washington				
Boeing 377	6.55	25,000 ceiling	— 5,500	"Stratocruiser"
Boeing 707	8.6	35,000 cruising 40,000 ceiling 45,000 maximum	— 5,000 — 7-8,000	Oxygen available for all passengers. If cabin altitude reaches 14,000' oxygen masks automatically drop down from above each seat.
Boeing 720	8.6	25-28,000 usual 40,000 ceiling 45,000 maximum	— 4,000 — 7,000	Available 1960. Maximum pressure release setting is 9.4 psi.
Bristol Aircraft Ltd. Filton House Bristol, England				
Britannia 100	7.25	Summer: 17,500-27,000 Winter: 21,500-31,000	— Sea Level to 5,000 — 2,000 to 7,000	First figures represent maximum speed operation; second for maximum range.
Britannia 300	8.3	Summer: 20,000-29,500 Winter: 22,000-32,000	— Sea Level to 4,000 — 1,000 to 5,000	Oxygen outlets for crew, plus 10 small portable oxygen bottles for passengers in cabin.
Canadair Post Office Box 6087 Montreal, Quebec				
Argonaut	4.16	14-17,000 usual 19,000 maximum*	— 8,000	*at normal load. However 29,000 is maximum at low load. Oxygen for crew: 4 outlets. BOAC added 4 portable oxygen units.
CL-44 (turbo-prop)	8.33	24-36,000 36,000 maximum*	— 8,000	*at normal load. Oxygen system designed in accordance with U. S. Civil requirements: CAR 4b para 46.651. It consists of a 300 psi liquid oxygen system, the oxygen stored in converters. Drop-down mask installations are available to all crew members and passengers.
Convair, a Division of General Dynamics Corp. San Diego, California				
Convair 240	3.75	8,000 16,000 maximum	— Sea Level — 6,000	Convairs are planned with oxygen outlets for 5 seats.
Convair 340	4.16* 4.0	9,000 16,000 maximum *17,000 ceiling	— Sea Level — 5,000 — 6,000	*Usual psi. *Temporary psi.
Convair 440	4.16	9,000 12-14,000 usual 20,000 maximum	— Sea Level — 5,000 — 8,000	Very rare.
Convair 880	8.2	21,000 35,000 cruising 40,000 maximum	— Sea Level — 6,000 — 8,000	
De Havilland Aircraft Company Limited Hatfield, Hertfordshire, England				
Comet 4	8.75	34,000 cruising 41,000 cruising 45,000 maximum	— 4,700 — 7,000 - - — 8,000 - -	Normal end of cruise. Under light weight and low temperature. BOAC plans to carry up to 8 portable oxygen sets per aircraft, supply rate up to 10 liters/min. Oxygen for crew.

TABLE (Continued)

Company & Aircraft	Δ psi	Operating Altitude	Cabin Altitude	Comments
Comet 4A		25,000 cruising	—4,000*	*Approximate. Since the 4A cruises at much lower altitude, a lower psi will be employed.
Douglas Aircraft Corp. Santa Monica, Calif.				
DC-3	0	10,000 ceiling	10,000	Unpressurized.
DC-4	0	10,000 ceiling	10,000	Unpressurized.
DC-6, 6B	4.16	18,000 usual 20,000 25,000 maximum	6,000 8,000 11,300	At above 25,000 the pressure differential gradually decreases.
DC-7	5.46	22,000	6,000	
DC-8	8.6	35,000 cruising 40,000 ceiling 45,000 maximum	— 5,000 — 7-8,000	Oxygen available for all passengers. If cabin altitude reaches 14,000' oxygen masks automatically drop down from above each seat.
Fairchild				
F-27	4.16	10-15,000 usual 20,000 ceiling	5-8,000 8,000	*Note some operators do not use full pressurization.
Glen L. Martin Co. Baltimore 3, Md.				
Martin 404	3.00	8-12,000	1,500 to 5,000	Flights under 300 miles.
		12-18,000	5-9,000	Flights over 300 miles.
Lockheed Aircraft Corporation Burbank, California				
Constellation	4.07	20,000 usual max.	8,000	All aircraft provided with oxygen outlets adjacent to each passenger seat, however masks are not normally carried for each passenger.
Super C* & G	5.36	20,000 usual max.	5,000	
Electra 188-A	6.55	25,000 usual max. 30,000 maximum	5,500 8,000	
Societe Des Avions Louis Breguet 24 Rue Georges Bizet Paris 16, France				
Breguet				
Sud Est Aviation 37 Boulevarde de Montmorency Paris 16, France				
Caravelle		25,000 40,000		
Armagnac				
Svenska Aeroplan AB Linkoping, Sweden				
Scandia	0			Unpressurized.
Vickers-Armstrong Aircraft Ltd. Weybridge, Surrey				
Viscount	6.5	30,000	8,000	Usual oxygen for crew plus portable apparatus to supply oxygen to individual passengers.
Viscount	4.5—5.0	15,000 cruising	3,000	As used by Capital Airlines.

* the 1649A provides the following:

1. Continuous flow outlets for 62 passengers, 4 relief crew members and 2 cabin attendants for 15 minutes.
2. Supplemental oxygen at 16,500' for active crew of 5 through diluter demand regulators.
3. A portable pressure demand type walk-around bottle with minimum of 300 liter capacity.

It is fair to say that 10,000 feet cabin altitude will seldom be exceeded except where an emergency occurs or where an accident such as decompression of the aircraft occurs. When such an internal altitude is exceeded, it is required by law that additional oxygen be supplied. Therefore a maximum of 10,000 feet external altitude is restored as soon as possible since oxygen cylinders reduce the payload. Although there are situations where this is not immediately possible such as a window fall out over the Rocky Mountains, yet it is generally accepted that this is an unlikely happening enough so that flight across the Rocky Mountains is considered safe. Particularly in four engine planes it is unlikely that the super charger providing the cabin differential would fail, since of the two super chargers in each plane, each is capable of maintaining the operating pressure in the cabin for practical purposes.

Of greater importance than the above factor is the question of standard operating practice among commercial airlines. It may be desired in extremely hot weather to decompress the plane relatively rapidly as soon as possible after takeoff to a cabin altitude of approximately 9,000 to 9,500 feet. This has the effect of allowing a rapid reduction of the internal cabin temperature and increasing the comfort of those passengers traveling. However, such an exposure might be a serious matter were certain patients with cardio-respiratory disease being carried on that particular flight. A second factor is that there is no automatic turning on of the maximum differential pressure but a gradual reaching of the final pressure at cruising altitude. This is to improve the comfort of the acclimatization. However, one can imagine that since modification of cabin altitude is possible, the maximum pressure differential may not always be reached at the set altitude. The practice will vary from airline to airline, but the information is readily obtainable from the companies, and modification is always possible.

In this report we are not concerned with the operational variables that we have mentioned. We are concerned, however, with the concept that

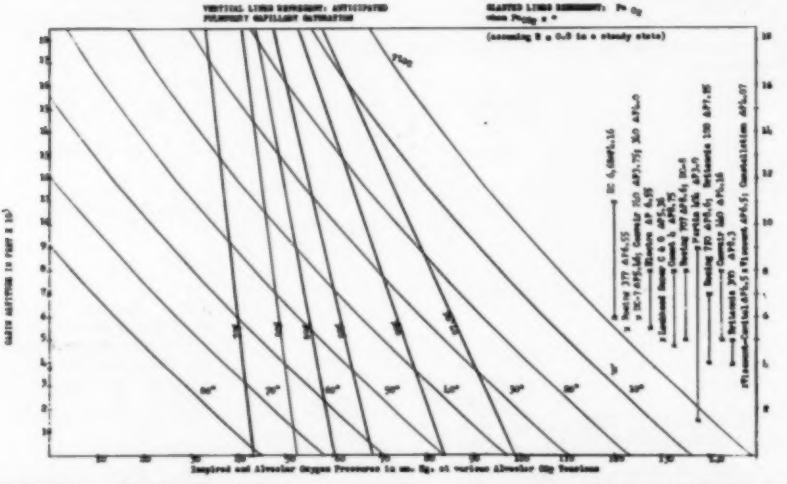

FIGURE 1: Master Chart. Pulmonary Capillary Saturation at Various Altitudes and Various Alveolar CO_2 Tensions.

if the maximum differential pressure between external and cabin altitude is reached and maintained throughout a flight and that no untoward happening should occur, how then should we separate those people who should travel in a given route on given equipment from those who should not.

Physiologic Considerations of Altitude

It stands to reason that a person traveling in a well pressurized aircraft over a set route across the American continent may well have a far lesser exposure to altitude and to need of movement around in such an aircraft than he would in standard surface travel. That is to say, it is fair that if a person can travel across the continent by train or bus, he can travel by air. However, it is probable that we are restricting travel altogether to too great an extent. Moreover, everybody does not travel such huge distances with such exposure to altitude. It is generally accepted that short distances of the order of 200 miles are probably best handled by surface transport, so that we are concerned with trips above 200 miles.

In the Master Chart (Figure 1) there is a study of what occurs at various altitudes to the pulmonary capillary saturation. This has been conceived in terms of cabin altitude and the ranges of a number of aircraft are shown in the right hand side of the drawing. The calculation is made on the basis that the patient is resting quietly in his airplane seat, and is breathing in such a way as to reach a steady state with a respiratory quotient of 0.8. It is further assumed that there is an all or none situation operating in the alveoli. By the all of none law, we mean that all factors in desaturation are to be considered as a venous admix-

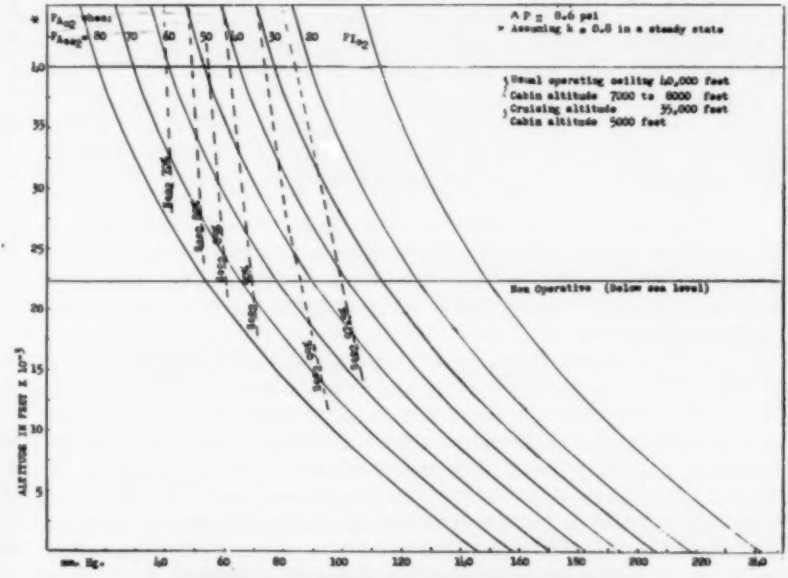
Usual operating ceiling 40,000 feet
Cabin altitude 7000 to 8000 feet
Cruising altitude 35,000 feet
Cabin altitude 5000 feet
Sea Operative (Below sea level)
ALTITUDE IN FEET X 10⁻³
mm. Hg.

FIGURE 2: BOEING 707 AND DOUGLAS DC-8

Note: Each aircraft requires its own curve to be calculated. A complete set has been made up covering the common commercial aircraft.

ture operation under certain defined conditions (see Wilson, R. H. L., *Stanford Medical Bulletin*, 15:47, 1957). That is to say, it is assumed that alveolar air and pulmonary capillary blood either completely come into equilibration or do not come into equilibration at all. Although such a method of considering the alveolar arterial gradient has definite limitations, it is perhaps more readily clinically accessible for the majority of the people. Such a patient is considered as having various alveolar CO_2 tensions.

Using such a graph, it is obvious that two things may happen:

1. In the presence of a raised CO_2 tension, a very considerable fall in pulmonary capillary saturation can be anticipated.
2. Where there is evidence of a diffusion gradient for oxygen, one can move along the inspired oxygen level (the X axis) to the left the required distance.

From examination of this chart, it would appear that those most seriously disabled by altitude will be those patients in whom there is CO_2 retention or a marked alveolar capillary block. As well, the patient who is unable to hyperventilate will be unable to produce a fall in his CO_2 tension and thus a rise in his pulmonary capillary saturation. On the other hand, such problems as fixed cardiac output in the absence of these other factors will not be of great importance. Restricted coronary blood flow may be of importance or not, depending upon the ability to hyperventilate and to reduce the alveolar CO_2 tension.

We are assuming information at sea level already obtained to remain valid and such concepts as the steady state to apply. We are ignoring such factors as diminished viscosity of air at altitude which may prove beneficial for example in emphysema. Even so, some concept of what is going to happen to the arterial saturation of a patient can be obtained by the use of this graph together with the separate graphs of each aircraft which are here made available. It is obvious that our concern for cardiac patients is far less than our concern for pulmonary patients. The only problem that remains is the interpretation of what is going on in the patient without the necessary studies that would have to be carried out to establish where the patient would stand at altitude.

The Clinical Assessment of Suitability for Air Transport

In patients with cardiopulmonary disease, the nature and severity of symptoms, the physical findings, the radiological findings, and in doubtful cases, certain chemical tests, make possible an adequate evaluation of altitude tolerance.

In *chronic pulmonary emphysema*, the presence of acidosis or impending acidosis is a relatively strong contraindication to altitude exposure. The important factors in these patients are the well known hazard of uncontrolled oxygen administration by unskilled personnel and the low pulmonary capillary blood oxygen saturations which may occur. If cyanosis, i.e., low blood oxygen saturation, is present, altitude exposure must be limited to 3,000 or 4,000 feet. Although direct transport on a DC-7 or Jetstream or Jet aircraft offers minimal time between San Francisco and New York, it would be adventageous for such a patient to go north to Seattle and to transfer to a Boeing 377 with its better cabin differential pressure yielding a lower cabin altitude for the final hop to New York.

Alternatively, a jet transport may be operating so far below its ceiling that pressurization can be maintained quite near sea level. It is in this matter that the cooperation of the airlines is going to be of the greatest importance. In the emphysematous patient without acidosis, the problem is less serious, unless marked cyanosis is present. In the patient with emphysema and no cyanosis except where there is gross restriction of ventilation, there appears to be little reason for concern.

In case of *restriction of ventilation* as caused by pulmonary or pleural fibrosis, it is necessary to consider the effect of ventilatory restriction upon the arterial oxygen saturation. In contradistinction to obstructive emphysema, it is safe to use added oxygen in these cases and respiratory acidosis is not a problem except in very advanced cases. The important factor in cases of restricted ventilation is the presence of cyanosis or arterial desaturation.

In patients with *alveolar capillary block*, there is a calculable lowering of the pulmonary capillary saturation. These patients may be divided for purposes of altitude tolerance into two groups: the first can increase ventilation, and the second cannot. It is safe for these patients to receive added oxygen throughout the exposure.

In patients with *coronary artery disease suspected or present in whom there is restricted ventilation*, it is a matter of considerable concern that the arterial oxygen saturation should not fall in air travel. Such patients are naturally candidates for administration of oxygen together with limited time exposure to the higher altitudes. In general, ho patient should be allowed to become altitude-hypoxic within eight weeks of an acute coronary occlusion, nor should a patient with angina fly without a supply of oxygen sufficient to restore the inspired oxygen tension to sea level or better. The *anemias* must be considered in relation to cardiac function, except for sickle cell anemia which presents its own specific problems.

In patients with *cardiac disease without failure, but with cyanosis*, the problem is maintaining the pulmonary capillary saturation by added oxygen. Ventilatory restriction is the most important coexisting disease contraindicating air travel. This group includes patients with arteriovenous shunts.

Lastly, in patients who are in *impending or actual cardiac failure, particularly on the left side*, the pulmonary capillary saturation may fall very easily and its maintenance is essential. The presence of any ventilatory restriction in such patients which is a remarkably likely thing to occur, should left-sided failure start to appear, is a fairly severe contraindication for air travel except with added oxygen from the beginning.

From the above, it seems clear that the disease and its severity is the important factor in deciding about air travel. Further, the factor of ability to increase ventilation, the possibility of depression of respiration by added oxygen, the presence or absence of cyanosis and other factors must be considered in making an estimate of the altitude tolerance and the duration of the exposure. The altitude at which the patient is living must be given due consideration.

Illness brought on by cardio-respiratory insufficiency aboard an aircraft in flight presents a serious therapeutic problem because of the ab-

sence of medical personnel, supplies, and breathing apparatus and of no little concern is the effect on the crew and passengers. Supplementary oxygen can be carried or is available on most aircraft. The value of prearrangement with the company cannot be overstressed and again consideration of the patient's condition can materially assist. Lastly, airsickness and anxiety must be avoided by all means possible in any patient with cardio-respiratory disability.

Suggested Approach of the Physician

It is clear that a positive recommendation as to safety would provide a difficult legal situation should in fact an accident occur after a recommendation had been made that any given altitude was safe for a specific patient. For this reason, the negative approach is thought desirable. That is to say, the phraseology should be that "Mr._____ should not be exposed to an altitude exceeding_____."

Arbitrarily we consider altitude exposure at cabin altitudes of:

I. Up to 10,000 feet.
II. Up to 8,000 feet.
III. Up to 6,000 feet.
IV. Up to 4,000 feet.
V. Up to 2,000 feet.

These correspond respectively in commercial air transport flying at their highest cruising range with:

I. Unpressurized aircraft, following the CAB ruling of above 10,000 feet, supplementary oxygen supply available.
II. Boeing 707 (Figure 2); 720.
Canadair: Argonaut; CL-44.
De Havilland: Comet 4; Dove.
Douglas: DC-6 and 6B; DC-8 (Figure 2).
Fairchild: F-27.
Lockheed: Constellation.
Martin 404 in flights over 300 miles.
Vickers: Viscount cruising at 30,000 feet.
III. All Jets flying at lower altitudes than maximum.
Boeing 377.
Britannia 100 in winter.
Convair 240; 340, 440; 880.
Douglas: DC-7.
Lockheed: Super C, G, H; Electra.
Martin 404 in flights under 300 miles.
IV. Britannia 100 in summer; Britannia 300.
De Havilland: Comet 4A.
Vickers: Viscount cruising at 15,000 feet.
V. Certain of the above aircraft flying lower altitude routes.

These are considered in terms of aircraft operating at their *high* cruising altitudes; in other words, near their operating ceilings. However, although these may apply on some long distance flights over mountainous terrain, they will not apply on many shorter flights, particularly where the terrain is flat. The presence of a particular type of airliner on a scheduled run should be interpreted as representing the maximal altitude reasonably likely to occur; in fact consultation with airlines

usually results in a reclassification of most flights to a considerably lower altitude.

We would recommend that no patient with suspected or symptomatic cardio-respiratory disease be exposed to altitude *Limit I*.

Mildly symptomatic disease without cardiac failure or marked ventilatory restriction should not be exposed above altitude *Limit II* (8,000 feet).

Recent (8 to 24 weeks after) myocardial infarction, clinical angina and sickle-cell anemia contraindicate travel above *Limit III* (6,000 feet), and individual supplementary oxygen supplies should be available for the patient. This should be continuously available during stops at airports such as Denver where the altitude exceeds 4,000 feet. The same oxygen proviso at *Limit III* applies to patients with alveolar capillary block who are cyanotic. This same limit restricts patients with pulmonary emphysema in whom only one of the triad of clinical cyanosis, cor pulmonale, and respiratory acidosis is present; where none of the triad is clinically present, extra oxygen need not be carried.

Limit IV applies to patients in Limit III where oxygen is not being carried, to those with more severe cardiac disease with marked cyanosis or recent decompensation, and to patients with pulmonary emphysema or other restrictive ventilatory disease in whom two of the triad of clinical cyanosis, cor pulmonale or respiratory acidosis are present.

Limit V applies to cardiac patients in failure or respiratory patients with all three manifestations and to myocardial infarction within 8 weeks.

It is recommended that air lines should be informed of the limit set by the physician at the time of purchase of the ticket. Where necessary, the medical department of such airlines can be consulted. In general, we would comment that airline medical personnel show considerable willingness to cooperate and help in these matters.

SUMMARY

We believe that a useful classification for planned air travel for patients with cardio-respiratory disease can be developed at a series of limiting altitudes ranging in 2,000 feet decrements from 10,000 feet to 2,000 feet in the cabin. By putting a limit, rather than making a recommendation of safety, it is felt that some of the objection to such a classification can be overcome. The time factor has not been accounted for at this time. A method of considering various aircraft, from the pulmonary physiologic point of view, is given together with some of the performance characteristics of certain aircraft in this regard. It is shown that respiratory acidosis and ventilatory restriction are perhaps the most important limiting factors with alveolar-capillary block as a less common consideration. It is felt that the average physician is in a position to classify patients. Such a classification moreover, could be useful to airlines accepting patients with cardio-respiratory disorders for air travel.

(The partial data summarized have been selected and compiled from sources believed to be reliable, but are not guaranteed as to accuracy or completeness either by the authors, the Journal, or the American College of Chest Physicians.)

RESUMEN

Creemos que una clasificación útil se podría hacer para pacientes con enfermedades cardio-respiratorias que desean viajar por aire, con reducciones de altitud de 2,000 pies — de 10,000 reduciendo — 2,000 pies a la vez. Poniendo un limite en vez de hacer una recomendación de seguridad, nos parece que algunas de las oposiciones a tal clasificación se podrían eliminar. El tiempo necesario hasta ahora no ha sido determinado. Un método de considerar various vehículos aereos por el punto de vista fisiológico de los pulmones sería conforme ciertos aereoplanos performan en estos casos. Una consideración menos común ha sido demostrada en que el acidosís respiratorio y la restricción ventilatoria son los factores limitantes mas importantes en "alveolar-capillary block." Sentimos que es el médico el llamado a clasificar estos pacientes. Tal clasificación, además, podría ser útil a las compañias aireas que acepten pacientes con enfermedades cardio-respiratorias para viajar por aire.

RESUMÉ

Nous pensons qu'une utile classification, pour l'organisation des voyages aeriens, des malades atteints de désordres cardio-respiratoire, peut être développée, par une sérieuse limitation d'altitude aux environs de 2,000 pieds par un décalage de 10,000 à 2,000 pieds, et dans les cabines, en limitant plutot qu'en recommandant la sécurite.

On est d'avis que les objections à une telle classification peuvent etre surmontées, le facteur temps ne rentrant pas en ligne de compte pour ce rapport.

Un moyen d'apprécier qu'il y a une science de la navigation aerienne au point de vue physiologique pulmonaire, est démontré par les caractéristiques des performances accomplies par certains appareils aériens, à cet effet.

Il est connu que les maladies cardio-respiratoires et respiration ventilatoire, de peut être les plus importantes du facteur limite, n'ont pas la moindre consideration commune avec le bloc alveolaire capillaire.

On est d'avis que le médecin moyen est en mesure d'opérer une classification des malades. Une telle classification peut être utile aux compagnies aériennes, exceptant les malades atteint de désordres cardio-respiratoires, des voyages aériens.

ZUSAMMENFASSUNGEN

Wir glauben dass eine brauchbare Klassifizierung des geplanten Luftverkehrs für patienten mit Kardio-respiratorischen Krankheiten entwicheit werden kann in einer serie von gemessenen Höhen die in 2,000′ verminderungen von 10,000′ bis 2,000′ in den Kabinen reichen.

Austatt der Empfohlung für Sicherheit dürften durch diese Beschránkungen manche Einwendungen gegen solche Klassifizierung überwáltigt werden, mit der Ausnahme des Zeitelements.

Eine methodische Betrachtung der verschiedenen Flugzeuge vom pulmonarischen-physiologischen Punkt aus ist angegeben zusammen mit einigen charakteristischen Ergenschaften sámtlicher Flugzeuge in dieser Bezichung.

Es ist festgestellt dass respiratorische acidosis und ventilatorische Restriktionen vielleicht die wichtigsten Elemente sind ausser dem alveolar-kapillarischen Block der weniger beaamt ist.

Wir glauben dass der durchschnittliche arzt seine Patienten so klassifizieren kann und dabei den Luftverkehrslinien behilflich sein kann in dem dass die patienten mit Kardio-respiratorischen Krankheiten für Flugverkehr akzeptiert werden können.

SECTION ON AVIATION MEDICINE
Committee on Physiologic Therapy
American College of Chest Physicians

Roger H. L. Wilson, San Francisco, California, *Chairman*
Robert B. Stonehill, Lackland AFB, Texas, *Secretary*
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Relationship Between Pulmonary Tuberculosis And Bronchial Asthma

Report of the Committee on Allergy
American College of Chest Physicians

Several questions have arisen on certain aspects of the relationship between pulmonary tuberculosis and allergic bronchial asthma. A questionnaire was sent to each member of the Committee on Allergy and replies have been received from 18 of the 34 members. A study of these answers and of the chairman's private patient cases reveals the following:

1. *Number of Cases* One can only approximate the number of patients who have typical allergic bronchial asthma plus active or quiescent pulmonary tuberculosis. A total of 150 cases was reported, including 18 from the chairman's practice.

The statistics show that about 1 per cent (one answer said 3 per cent and another 5 per cent) of patients with predominant pulmonary tuberculosis also have bronchial asthma. On the other hand, the majority of the committee feel that less than 1 per cent of patients with predominant bronchial asthma have or have had definite pulmonary tuberculosis. An El Paso member of the committee, however, reports that about 20 per cent of his asthmatics have an associated tuberculosis. He goes on to say that this 20 per cent were already tuberculous patients in a sanatarium; and that this occurred in the days before streptomycin and other antibiotics. He further states that he now has only the usual 1 per cent approximately of patients with asthma who develop tuberculosis and vice versa of patients with tuberculosis who develop asthma.

2. *Age and Sex* Adults predominate in those who have both. The chairman has one child of five who has apparently just recovered from pulmonary tuberculosis and who also has bronchial asthma; another member reports the combination in a child of eight. The rest of the cases, however, range from about 16 to 75. Of the cases reported as to sex, 21 were males, 25 females.

3. *Effect of Pulmonary Tuberculosis on the Asthma* Accurate answers to this question are rather difficult, but four members stated that tuberculosis seems harmful to the asthma. Eight believed that no harm results.

4. *Effect of Bronchial Asthma on Pulmonary Tuberculosis* One member felt that the asthma lessened the prognosis as regards the tuberculosis. Five stated that no effect occurred.

5. *Use of ACTH and Steroids* ACTH and steroids are now being used in patients who have both bronchial asthma and quiescent or active pulmonary tuberculosis. In such cases, of course, the usual anti-tuberculosis therapy, especially streptomycin, is also employed.

The committee members gave some interesting information; of those who replied, four do not use ACTH, while six do. Those who use it are enthusiastic about it, and one of the committee replied that one of his two patients would have died without ACTH and steroids, and that patient's tuberculosis seemed no worse. In the chairman's experience,

ACTH has been used in five cases. In one patient with open tuberculosis, her asthma was so severe that death seemed imminent. Two liters of glucose each with 20 units of ACTH brought prompt and gratifying relief, and her tuberculosis did not seem aggravated. In four other patients with a little less severe status asthmaticus, ACTH was also used, and in each case the asthmatic seizure cleared and the tuberculosis was not increased in three; tubercle bacilli re-appeared in the sputum of the fourth patient.

Cortisone and Prednisone According to some members of the committee, these drugs may be somewhat more dangerous, probably because these steroids are used over longer periods. One member of our committee reported that quiescent tuberculosis became active in two of his six cases. Another prefers ACTH to the steroids. In recent literature, other observers have reported activation or re-activation when steroids were employed.

The chairman's statistics show that after cortisone was given, tubercle bacilli re-appeared in two cases. In another patient in whom tuberculosis was suspected, the bacilli were first found shortly after cortisone was started; in this patient, no bacilli were found in six previous examinations of the sputum.

SUMMARY

The Committee on Allergy of the American College of Chest Physicians reports a statistical relationship between pulmonary tuberculosis and bronchial asthma. The following findings seem apparent after reviewing 150 patients in whom allergic bronchial asthma was associated with active or quiescent pulmonary tuberculosis.

1. About one per cent of patients with predominant pulmonary tuberculosis also have allergic bronchial asthma; an even smaller percentage of those with predominant bronchial asthma have or have had pulmonary tuberculosis.

2. Most patients who have both were adults; there is little distinction as regards sex.

3. A minority of the committee feels that bronchial asthma lessens the prognosis as regards co-existing pulmonary tuberculosis, and vice versa. The majority believes that neither condition has any important effect on the other.

4. ACTH should be given patients with severe uncontrollable status asthmaticus even though such patients also have active or quiescent pulmonary tuberculosis. A minority of the committee dissents from this view. It is understood that streptomycin, etc., should also be used in such cases. The ACTH may be life-saving. In most cases the tuberculosis does not seem to be aggravated.

5. Cortisone and prednisone are usually given over longer periods and therefore must be given more cautiously. If severe asthma persists, however, prednisone may well be used, along with anti-tuberculosis therapy.

COMMITTEE ON ALLERGY

American College of Chest Physicians

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Editorial

Clinical Roentgenographic Examination of the Chest

In recent years, a great confusion has arisen between survey examination of the chest by the single film technique of various types and clinical roentgenographic examination of the chest. The first type of examination, is of course indicated for patients without symptoms who are being studied merely to demonstrate the presence of a lesion. Unfortunately this has become confused with the radiological exploration of a patient with symptoms. In many cases, a single posteroanterior study of the chest is being regarded as an adequate evaluation of a patient with chest symptoms. This is most unsatisfactory and does great damage both to the patient involved and to the understanding of the contributions of radiologic exploration of the chest. On innumerable occasions, such single posteroanterior films of the chest have not permitted proper evaluation of the early manifestations of bronchogenic carcinoma, due to the inadequate information available in this type study. On other numerous occasions, significant evidence of active pulmonary tuberculosis has not been demonstrated because of this inadequate roentgen approach. In particular, numerous evidences of caseous pneumonic pulmonary tuberculosis of the superior segments of the left lower lobe with regional cavitation have not been properly visualized as well as numerous manifestations of the segmental apical tuberculosis involving the upper lobes.

There is a universal desire to diagnose pulmonary disease both accurately and early in its course. Proper roentgen evaluation is an essential component in establishing such early and accurate diagnosis. In view of the many inadequate roentgen evaluations of the chest that are being performed, it is essential to emphasize the value of a careful clinical study of the chest by radiologic technique including fluoroscopy, by lordotic apical study, by inspiratory, expiratory study, by studies in the lateral and other planes as indicated. It is important to emphasize that this basic conventional technique is necessary and desirable before attempts are made to explore the chest by other techniques such as sectional radiography, bronchography, angiography and bronchoscopy.

Bronchography is a valuable tool whose contributions are not sufficiently emphasized. It is a great aid to the diagnosis of pulmonary disease other than bronchiectasis. It has been our experience that it may be a valuable tool in diagnosis of peripheral bronchogenic carcinoma. Greater efforts to employ it are extremely desirable.

It is important in addition, to emphasize that precise anatomic, pathologic and etiologic conclusions may be reached by careful clinical radiography of the chest. While it is true, that in certain cases, such precise data is not available by radiologic means alone, in a high percentage of cases when proper clinical correlation is obtained, such conclusions may be obtained radiographically. Due to the fact that in certain cases of pulmonary tuberculosis, final conclusions cannot be reached until the

tubercle bacilli are demonstrated in the sputum, there has been an unfortunate tendency to generalize from this to all types of radiologic evaluation of the chest. This is not justified.

In addition, the greater the information that is obtained from the initial conventional study of the chest, the lower the cost of the total medical exploration to the patient and the less marked is the radiation exposure required.

These facts certainly justify a universal reevaluation of the contributions and techniques of clinical roentgenography of the chest.

PAUL S. FRIEDMAN, M.D., F.C.C.P.
Philadelphia, Pennsylvania

The President's Page

WHEN MEDICINE CROSSES FRONTIERS ON THE PERSONAL LEVEL

Modern medicine at the present time is, to put the matter in the kindliest possible way, very independent. We have little to do with the professional efforts of our colleagues in other countries. Indeed, the footnotes in current medical journals would suggest that we are largely unacquainted with such efforts. Instead of reading foreign medical journals, we dismiss them too frequently with an easy stereotype. We do not bother to keep up with one country because they have made notable mistakes in the past. We conclude that scientists of another are imitative and that still others are backward. Furthermore, there are manifest differences in the character of patient populations which would make the observations of doctors from other countries invalid for us even if they could be depended upon. Hence we are spared the necessity of seeing what those observations might be.

This is not provincialism in its true sense even if its result is a provincial medicine. The doctor is not a nationalist in his medicine because of any general conviction about local superiority, but because it is a difficult matter to cross national boundaries with confidence and judgment. England and the United States, for instance, are perhaps as close culturally as any two nations of the world, but the British medical journal is notably different from its American counterpart. There are differences in style and differences in methods of reporting. Where such a close cultural affinity does not exist, these differences are magnified, and they are further compounded by problems of language. These differences are a barrier because they make it difficult to apply the criteria by which we usually judge the value and reliability of research reported. The obvious and easy thing to do in this case is to reject.

The easiest way to break through this barrier is to get to know personally workers from other countries. This is the *raison d'etre* of international meetings, and their popularity in recent years suggests that they are successful in this aim, as demonstrated by the International Congresses of the American College of Chest Physicians. In the first place, those attending such meetings shortly discover that every nation has its quota of first rate medical men. The qualities of insight and dedication and professional competence that may be obscured by different customs in written communication are immediately apparent when men meet face to face. The personal contacts made in a brief international meeting can establish a mutual confidence that will last a lifetime.

In the second place, such meetings offer an opportunity to understand the differences in point of view which have hitherto been a barrier to understanding. When papers are presented in other languages, translations are immediately made available. The discussion periods which follow can then be used to clarify points and clear up possible sources of misunderstanding. The sometimes elementary differences which make written communication often difficult can be cleared up in a moment, and we are thereafter in a position to understand subsequent written communication.

Furthermore, through such personal contacts we can learn to positively value the differences in approach that exist from one country to another. The differences in patient population that exist can be of great value. For example, the declining tuberculosis rates in the United States are sure to make diagnosis of the disease, with its extraordinary diversity of manifestations, increasingly difficult. Few doctors in the United States at the present time see enough tuberculosis to be really familiar with its protean manifestations. Hence, even a single visit to a clinic in a country where the disease is common can be of inestimable value. Those of us who were fortunate enough to be invited to visit tuberculosis sanatoria in Japan two years ago learned more about tuberculosis than we could have in several years of practice in the United States. There is also great value in seeing clinical entities which have hitherto been "textbook diseases" for some countries. This can be useful; as everyone, doctors and patients, travel incessantly these days, unusual diseases are certain to be brought home from time to time.

The doctor will, of course, think of the advantages of international travel primarily in terms of the professional advantages which can be realized. As anyone who has attended an international meeting can testify, these are great. (It is lamentable that some countries do not realize this, and so regulate the export of their currencies that such travel of doctors and scientists is nearly prohibited.) But it should perhaps be pointed out that in addition, doctors are the finest kind of ambassadors. United to one another by their common science, they are admirably suited to understand one another and to make themselves understood. And their most profound professional commitment is to the education of disease regardless of race, creed or color. When medicine crosses frontiers on the personal level everybody gains.

Seymour M. Farber

26th ANNUAL MEETING

The 26th Annual Meeting of the American College of Chest Physicians will be held at the Saxony Hotel, Miami Beach, June 8-12, just preceding the 109th meeting of the American Medical Association, June 13-17. The complete program for the College meeting appeared in the April issue of **Diseases of the Chest.** Additional copies of the program may be obtained by writing to the Executive Offices of the College, 112 East Chestnut Street, Chicago 11, Illinois.

The interesting and extensive scientific program and special functions planned for this session will make a visit to Miami Beach worthwhile and enjoyable.

CHAPTER NEWS

VENEZUELA CHAPTER

Seated, left to right: Drs. Pedro Iturbe, Governor of the College for Zulia Province; Luis Gomez Lopez, Henry C. Sweany, Mt. Vernon, Missouri; Jose Ignacio Baldo, Regent of the College for Venezuela; Cesar Rodriguez and Rogelio Valladares. Standing, left to right: Drs. Francisco Ruscalleda, Ruben Jonckheer, Carlos Ortega, Vice-President, Venezuela Chapter; Alejandro Principe, Secretary, Venezuela Chapter; Rafael Gallardo, Humberto Delgado Rivas, Vice-President, Venezuela Chapter; Ladislao Pollak, Ramon Soto Matos, Manuel Adrianza, Paulo Emilio Marquez and Juvenal Curiel.

The Venezuela Chapter of the College held a breakfast meeting on December 11 in Valencia, Venezuela, during the Fifth Venezuelan Congerss on Tuberculosis, December 8-12. Dr. Henry C. Sweany, Mt. Vernon, Missouri, represented the President of the College at the meeting. After a discussion of the national plan for studying the mycoses in Venezuela, Dr. Sweany spoke on his impressions of the work being done by tuberculosis specialists in Venezuela.

A business meeting of the chapter followed, at which the following officers were elected:

President	Humberto Delgado Rivas, Maracaibo
Vice-President	Carlos Ortega, Valencia
Secretary-Treasurer	Alejandro Principe, Caracas

NEW CHAPTER OFFICERS

CALIFORNIA CHAPTER

President	Samuel J. Sills, Los Angeles
Vice-President	John Mack Baker, Sacramento
Secretary-Treasurer	Francis J. Curry, San Francisco

CUBAN CHAPTER

President	Rogelio Barata, Havana
Vice-President	Clemente Rodriguez Remus, Havana
Secretary-Treasurer	Manuel Conde Lopez, Havana

FLORIDA CHAPTER

President	Ivan C. Schmidt, West Palm Beach
Vice-President	Charles F. Tate, Jr., Coral Gables
Secretary-Treasurer	Harold W. Johnston, Orlando

HONG KONG AND MACAU CHAPTER

President	A. S. Moodie, Hong Kong
Vice-President	Hee Chee Chan, Hong Kong (re-elected)
Secretary-Treasurer	Phyllis Haddow, Hong Kong (re-elected)

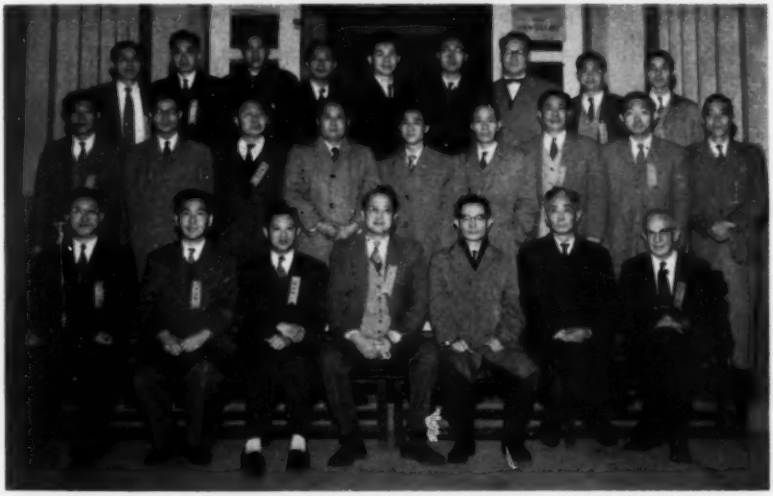
MISSOURI CHAPTER

President	John C. Murphy, St. Louis
Vice-President	Herbert C. Sweet, St. Louis
Secretary-Treasurer	David Nafe Kerr, St. Louis (re-elected)

PACIFIC NORTHWEST CHAPTER

President	Edward H. Morgan, Seattle, Washington
Vice-President	J. Karl Poppe, Portlan, Oregon
Secretary-Treasurer	Norman Arcese, Seattle, Washington

REPUBLIC OF CHINA CHAPTER



First row, left to right: Drs. Y. S. Huang, Sze-Piao Yang, Governor of the College for Republic of China; John Chen, Secretary-Treasurer of the Republic of China Chapter; C. T. Hsing, Chapter President; H. T. Lin, Chapter Vice-President; T. K. Chang and Alan H. Penington. Second row, left to right: Dr. K. Y. Hsu, P. H. Hu, G. S. Chang, I. M. Hao, C. K. Chen, H. W. Luan, Jr., T. Y. Lin, T. L. Su and K. S. Lu. Third row, left to right: H. T. Chen, H. C. Chao, Y. T. Tsu, C. W. Chao, T. C. Fuh, H. T. Tien, L. C. Chiang, B. J. Lee and W. F. Cheng.

The Republic of China Chapter was officially organized at a meeting held in the Taipei Tuberculosis Control Center, Taipei, Taiwan, on February 12. Dr. Sze-Piao Yang, Chief of the Chest Service at the National Taiwan University Hospital and Governor for the College, presided and gave the opening address. The following officers were elected:

President	C. T. Hsing, Taipei
Vice-President	H. T. Lin, Taipei
Secretary-Treasurer	John Yueh-Han Chen, Taipei

At the close of the meeting, members of the College and their guests attended a dinner given by Dr. Alan H. Pennington, and Dr. Yang.

ERRATUM

In the paper entitled "The Influence of Instrumental Resistance on the Maximum Breathing Capacity" by Zwi, Theron, McGregor and Beckdale (XXXVI, No. 4, October), the lines X and Y in Figures 2 and 3, representing the data obtained by McKerrow, have been incorrectly plotted. The correct values for these lines may be obtained by reference to the original article by McKerrow.

MEDICAL SERVICE BUREAU

POSITIONS AVAILABLE

Assistant Medical Director wanted for a county hospital in upstate New York. Applicant must have New York state license or be eligible for same and have at least three years' responsible experience in tuberculosis. Salary range is $8215 to $9915, plus complete family maintenance (home, food, etc.). Please address inquiries to Box 304A, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Immediate opening for resident physician, eligible for Indiana license. Tuberculosis experience not necessary. Salary range $9,000 to $11,400 with complete maintenance. Contact: P. H. Becker, M. D., Superintendent, Parramore Hospital, Crown Pont, Indiana.

CALENDAR OF EVENTS

National and International Meetings
26th Annual Meeting, American College of Chest Physicians
Miami Beach, Florida, June 8-12, 1960

Sixth International Congress on Diseases of the Chest
Council on International Affairs
American College of Chest Physicians
Vienna, Austria, August 27 - September 1, 1960

CHAPTER MEETINGS

New Jersey Chapter, Atlantic City, May 18

New Mexico Chapter, Albuquerque, May 18

Ohio Chapter, Cleveland, May 18

Oklahoma Chapter, Sequoyah State Park, May 18-19

Illinois Chapter, Chicago, May 26

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